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## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>C12N 15/12, A61K 38/17, C07K 14/47, 16/18, A61K 35/14</b>		<b>A2</b>	(11) International Publication Number: <b>WO 99/38973</b> (43) International Publication Date: <b>5 August 1999 (05.08.99)</b>																					
(21) International Application Number: <b>PCT/US99/01642</b> (22) International Filing Date: <b>26 January 1999 (26.01.99)</b> (30) Priority Data: <table border="0"><tr><td>09/015,029</td><td>28 January 1998 (28.01.98)</td><td>US</td></tr><tr><td>09/015,022</td><td>28 January 1998 (28.01.98)</td><td>US</td></tr><tr><td>09/040,828</td><td>18 March 1998 (18.03.98)</td><td>US</td></tr><tr><td>09/040,831</td><td>18 March 1998 (18.03.98)</td><td>US</td></tr><tr><td>09/122,192</td><td>23 July 1998 (23.07.98)</td><td>US</td></tr><tr><td>09/122,191</td><td>23 July 1998 (23.07.98)</td><td>US</td></tr><tr><td>09/219,245</td><td>22 December 1998 (22.12.98)</td><td>US</td></tr></table>		09/015,029	28 January 1998 (28.01.98)	US	09/015,022	28 January 1998 (28.01.98)	US	09/040,828	18 March 1998 (18.03.98)	US	09/040,831	18 March 1998 (18.03.98)	US	09/122,192	23 July 1998 (23.07.98)	US	09/122,191	23 July 1998 (23.07.98)	US	09/219,245	22 December 1998 (22.12.98)	US	(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
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(54) Title: <b>COMPOUNDS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER AND METHODS FOR THEIR USE</b>																								
(57) Abstract <p>Compounds and methods for treating lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or polynucleotides encoding such polypeptides, are also provided, together with polynucleotides for preparing the inventive polypeptides.</p>																								

## COMPOUNDS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER AND METHODS FOR THEIR USE

### 5 TECHNICAL FIELD

The present invention relates generally to compositions and methods for the treatment of lung cancer. The invention is more specifically related to nucleotide sequences that are preferentially expressed in lung tumor tissue, together with polypeptides encoded by such nucleotide sequences. The inventive nucleotide sequences and polypeptides may be used  
10 in vaccines and pharmaceutical compositions for the treatment of lung cancer.

### BACKGROUND OF THE INVENTION

Lung cancer is the primary cause of cancer death among both men and women in the U.S., with an estimated 172,000 new cases being reported in 1994. The five-year  
15 survival rate among all lung cancer patients, regardless of the stage of disease at diagnosis, is only 13%. This contrasts with a five-year survival rate of 46% among cases detected while the disease is still localized. However, only 16% of lung cancers are discovered before the disease has spread.

Early detection is difficult since clinical symptoms are often not seen until the  
20 disease has reached an advanced stage. Currently, diagnosis is aided by the use of chest x-rays, analysis of the type of cells contained in sputum and fiberoptic examination of the bronchial passages. Treatment regimens are determined by the type and stage of the cancer, and include surgery, radiation therapy and/or chemotherapy. In spite of considerable research into therapies for the disease, lung cancer remains difficult to treat.

25 Accordingly, there remains a need in the art for improved vaccines, treatment methods and diagnostic techniques for lung cancer.

### SUMMARY OF THE INVENTION

Briefly stated, the present invention provides compounds and methods for the  
30 therapy of lung cancer. In a first aspect, isolated polynucleotides encoding lung tumor polypeptides are provided, such polynucleotides comprising a nucleotide sequence selected

herein; and (b) detecting in the sample a protein or polypeptide that binds to the binding agent. In preferred embodiments, the binding agent is an antibody, most preferably a monoclonal antibody.

In related aspects, methods are provided for monitoring the progression of lung cancer in a patient, comprising: (a) contacting a biological sample obtained from a patient with a binding agent that is capable of binding to one of the polypeptides disclosed herein; (b) determining in the sample an amount of a protein or polypeptide that binds to the binding agent; (c) repeating steps (a) and (b); and comparing the amounts of polypeptide detected in steps (b) and (c).

Within related aspects, the present invention provides antibodies, preferably monoclonal antibodies, that bind to the inventive polypeptides, as well as diagnostic kits comprising such antibodies, and methods of using such antibodies to inhibit the development of lung cancer.

The present invention further provides methods for detecting lung cancer comprising: (a) obtaining a biological sample from a patient; (b) contacting the sample with a first and a second oligonucleotide primer in a polymerase chain reaction, at least one of the oligonucleotide primers being specific for a polynucleotide that encodes one of the polypeptides disclosed herein; and (c) detecting in the sample a DNA sequence that amplifies in the presence of the first and second oligonucleotide primers. In a preferred embodiment, at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of a polynucleotide comprising a sequence selected from the group consisting of SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181.

In a further aspect, the present invention provides a method for detecting lung cancer in a patient comprising: (a) obtaining a biological sample from the patient; (b) contacting the sample with an oligonucleotide probe specific for a polynucleotide that encodes one of the polypeptides disclosed herein; and (c) detecting in the sample a DNA sequence that hybridizes to the oligonucleotide probe. Preferably, the oligonucleotide probe comprises at least about 15 contiguous nucleotides of a polynucleotide comprising a sequence selected from the group consisting of SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181. In related aspects, diagnostic kits comprising the above oligonucleotide probes or primers are provided.

- SEQ ID NO: 14 is the determined cDNA sequence for L355C1.cons  
SEQ ID NO: 15 is the determined cDNA sequence for L366C1.cons  
SEQ ID NO: 16 is the determined cDNA sequence for L163C1a  
SEQ ID NO: 17 is the determined cDNA sequence for LT86-1  
5 SEQ ID NO: 18 is the determined cDNA sequence for LT86-2  
SEQ ID NO: 19 is the determined cDNA sequence for LT86-3  
SEQ ID NO: 20 is the determined cDNA sequence for LT86-4  
SEQ ID NO: 21 is the determined cDNA sequence for LT86-5  
SEQ ID NO: 22 is the determined cDNA sequence for LT86-6  
10 SEQ ID NO: 23 is the determined cDNA sequence for LT86-7  
SEQ ID NO: 24 is the determined cDNA sequence for LT86-8  
SEQ ID NO: 25 is the determined cDNA sequence for LT86-9  
SEQ ID NO: 26 is the determined cDNA sequence for LT86-10  
SEQ ID NO: 27 is the determined cDNA sequence for LT86-11  
15 SEQ ID NO: 28 is the determined cDNA sequence for LT86-12  
SEQ ID NO: 29 is the determined cDNA sequence for LT86-13  
SEQ ID NO: 30 is the determined cDNA sequence for LT86-14
- 
- SEQ ID NO: 31 is the determined cDNA sequence for LT86-15  
SEQ ID NO: 32 is the predicted amino acid sequence for LT86-1  
20 SEQ ID NO: 33 is the predicted amino acid sequence for LT86-2  
SEQ ID NO: 34 is the predicted amino acid sequence for LT86-3  
SEQ ID NO: 35 is the predicted amino acid sequence for LT86-4  
SEQ ID NO: 36 is the predicted amino acid sequence for LT86-5  
SEQ ID NO: 37 is the predicted amino acid sequence for LT86-6  
25 SEQ ID NO: 38 is the predicted amino acid sequence for LT86-7  
SEQ ID NO: 39 is the predicted amino acid sequence for LT86-8  
SEQ ID NO: 40 is the predicted amino acid sequence for LT86-9  
SEQ ID NO: 41 is the predicted amino acid sequence for LT86-10  
SEQ ID NO: 42 is the predicted amino acid sequence for LT86-11  
30 SEQ ID NO: 43 is the predicted amino acid sequence for LT86-12



- SEQ ID NO: 74 is the predicted amino acid sequence for LT86-21  
SEQ ID NO: 75 is the predicted amino acid sequence for LT86-22  
SEQ ID NO: 76 is the predicted amino acid sequence for LT86-26  
SEQ ID NO: 77 is the predicted amino acid sequence for LT86-27  
5 SEQ ID NO: 78 is the determined extended cDNA sequence for L86S-12  
SEQ ID NO: 79 is the determined extended cDNA sequence for L86S-36  
SEQ ID NO: 80 is the determined extended cDNA sequence for L86S-46  
SEQ ID NO: 81 is the predicted extended amino acid sequence for L86S-12  
SEQ ID NO: 82 is the predicted extended amino acid sequence for L86S-36  
10 SEQ ID NO: 83 is the predicted extended amino acid sequence for L86S-46  
SEQ ID NO: 84 is the determined 5' cDNA sequence for L86S-6  
SEQ ID NO: 85 is the determined 5' cDNA sequence for L86S-11  
SEQ ID NO: 86 is the determined 5' cDNA sequence for L86S-14  
SEQ ID NO: 87 is the determined 5' cDNA sequence for L86S-29  
15 SEQ ID NO: 88 is the determined 5' cDNA sequence for L86S-34  
SEQ ID NO: 89 is the determined 5' cDNA sequence for L86S-39  
SEQ ID NO: 90 is the determined 5' cDNA sequence for L86S-47  
SEQ ID NO: 91 is the determined 5' cDNA sequence for L86S-49  
SEQ ID NO: 92 is the determined 5' cDNA sequence for L86S-51  
20 SEQ ID NO: 93 is the predicted amino acid sequence for L86S-6  
SEQ ID NO: 94 is the predicted amino acid sequence for L86S-11  
SEQ ID NO: 95 is the predicted amino acid sequence for L86S-14  
SEQ ID NO: 96 is the predicted amino acid sequence for L86S-29  
SEQ ID NO: 97 is the predicted amino acid sequence for L86S-34  
25 SEQ ID NO: 98 is the predicted amino acid sequence for L86S-39  
SEQ ID NO: 99 is the predicted amino acid sequence for L86S-47  
SEQ ID NO: 100 is the predicted amino acid sequence for L86S-49  
SEQ ID NO: 101 is the predicted amino acid sequence for L86S-51  
SEQ ID NO: 102 is the determined DNA sequence for SLT-T1  
30 SEQ ID NO: 103 is the determined 5' cDNA sequence for SLT-T2

- SEQ ID NO: 134 is the determined cDNA sequence for PSLT-69  
SEQ ID NO: 135 is the determined cDNA sequence for PSLT-71  
SEQ ID NO: 136 is the determined cDNA sequence for PSLT-73  
SEQ ID NO: 137 is the determined cDNA sequence for PSLT-79  
5 SEQ ID NO: 138 is the determined cDNA sequence for PSLT-03  
SEQ ID NO: 139 is the determined cDNA sequence for PSLT-09  
SEQ ID NO: 140 is the determined cDNA sequence for PSLT-011  
SEQ ID NO: 141 is the determined cDNA sequence for PSLT-041  
SEQ ID NO: 142 is the determined cDNA sequence for PSLT-62  
10 SEQ ID NO: 143 is the determined cDNA sequence for PSLT-6  
SEQ ID NO: 144 is the determined cDNA sequence for PSLT-37  
SEQ ID NO: 145 is the determined cDNA sequence for PSLT-74  
SEQ ID NO: 146 is the determined cDNA sequence for PSLT-010  
SEQ ID NO: 147 is the determined cDNA sequence for PSLT-012  
15 SEQ ID NO: 148 is the determined cDNA sequence for PSLT-037  
SEQ ID NO: 149 is the determined 5' cDNA sequence for SAL-3  
SEQ ID NO: 150 is the determined 5' cDNA sequence for SAL-24  
SEQ ID NO: 151 is the determined 5' cDNA sequence for SAL-25  
SEQ ID NO: 152 is the determined 5' cDNA sequence for SAL-33  
20 SEQ ID NO: 153 is the determined 5' cDNA sequence for SAL-50  
SEQ ID NO: 154 is the determined 5' cDNA sequence for SAL-57  
SEQ ID NO: 155 is the determined 5' cDNA sequence for SAL-66  
SEQ ID NO: 156 is the determined 5' cDNA sequence for SAL-82  
SEQ ID NO: 157 is the determined 5' cDNA sequence for SAL-99  
25 SEQ ID NO: 158 is the determined 5' cDNA sequence for SAL-104  
SEQ ID NO: 159 is the determined 5' cDNA sequence for SAL-109  
SEQ ID NO: 160 is the determined 5' cDNA sequence for SAL-5  
SEQ ID NO: 161 is the determined 5' cDNA sequence for SAL-8  
SEQ ID NO: 162 is the determined 5' cDNA sequence for SAL-12  
30 SEQ ID NO: 163 is the determined 5' cDNA sequence for SAL-14

- SEQ ID NO: 194 is the predicted amino acid sequence for SAL-5  
SEQ ID NO: 195 is the predicted amino acid sequence for SAL-8  
SEQ ID NO: 196 is the predicted amino acid sequence for SAL-12  
SEQ ID NO: 197 is the predicted amino acid sequence for SAL-14  
5 SEQ ID NO: 198 is the predicted amino acid sequence for SAL-16  
SEQ ID NO: 199 is the predicted amino acid sequence for SAL-23  
SEQ ID NO: 200 is the predicted amino acid sequence for SAL-26  
SEQ ID NO: 201 is the predicted amino acid sequence for SAL-29  
SEQ ID NO: 202 is the predicted amino acid sequence for SAL-32  
10 SEQ ID NO: 203 is the predicted amino acid sequence for SAL-39  
SEQ ID NO: 204 is the predicted amino acid sequence for SAL-42  
SEQ ID NO: 205 is the predicted amino acid sequence for SAL-43  
SEQ ID NO: 206 is the predicted amino acid sequence for SAL-44  
SEQ ID NO: 207 is the predicted amino acid sequence for SAL-48  
15 SEQ ID NO: 208 is the predicted amino acid sequence for SAL-68  
SEQ ID NO: 209 is the predicted amino acid sequence for SAL-72  
SEQ ID NO: 210 is the predicted amino acid sequence for SAL-77  
SEQ ID NO: 211 is the predicted amino acid sequence for SAL-86  
SEQ ID NO: 212 is the predicted amino acid sequence for SAL-88  
20 SEQ ID NO: 213 is the predicted amino acid sequence for SAL-93  
SEQ ID NO: 214 is the predicted amino acid sequence for SAL-100  
SEQ ID NO: 215 is the predicted amino acid sequence for SAL-105  
SEQ ID NO: 216 is a second predicted amino acid sequence for SAL-50

## 25 DETAILED DESCRIPTION OF THE INVENTION

As noted above, the present invention is generally directed to compositions and methods for the therapy of lung cancer. The compositions described herein include polypeptides, fusion proteins and polynucleotides. Also included within the present invention are molecules (such as an antibody or fragment thereof) that bind to the inventive  
30 polypeptides. Such molecules are referred to herein as "binding agents."

of the proteins described herein may be identified in antibody binding assays. Such assays may generally be performed using any of a variety of means known to those of ordinary skill in the art, as described, for example, in Harlow and Lane, *Antibodies: A Laboratory Manual*, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY, 1988. For example, a polypeptide  
5 may be immobilized on a solid support (as described below) and contacted with patient sera to allow binding of antibodies within the sera to the immobilized polypeptide. Unbound sera may then be removed and bound antibodies detected using, for example, <sup>125</sup>I-labeled Protein A. Alternatively, a polypeptide may be used to generate monoclonal and polyclonal antibodies for use in detection of the polypeptide in blood or other fluids of lung cancer  
10 patients. Methods for preparing and identifying immunogenic portions of antigens of known sequence are well known in the art and include those summarized in Paul, *Fundamental Immunology*, 3<sup>rd</sup> ed., Raven Press, 1993, pp. 243-247.

The term "polynucleotide(s)," as used herein, means a single or double-stranded polymer of deoxyribonucleotide or ribonucleotide bases and includes DNA and  
15 corresponding RNA molecules, including HnRNA and mRNA molecules, both sense and anti-sense strands, and comprehends cDNA, genomic DNA and recombinant DNA, as well as wholly or partially synthesized polynucleotides. An HnRNA molecule contains introns and corresponds to a DNA molecule in a generally one-to-one manner. An mRNA molecule corresponds to an HnRNA and DNA molecule from which the introns have been excised. A  
20 polynucleotide may consist of an entire gene, or any portion thereof. Operable anti-sense polynucleotides may comprise a fragment of the corresponding polynucleotide, and the definition of "polynucleotide" therefore includes all such operable anti-sense fragments.

The compositions and methods of the present invention also encompass variants of the above polypeptides and polynucleotides.

25 A polypeptide "variant," as used herein, is a polypeptide that differs from the recited polypeptide only in conservative substitutions and/or modifications, such that the antigenic properties of the polypeptide are retained. In a preferred embodiment, variant polypeptides differ from an identified sequence by substitution, deletion or addition of five amino acids or fewer. Such variants may generally be identified by modifying one of the  
30 above polypeptide sequences, and evaluating the antigenic properties of the modified polypeptide using, for example, the representative procedures described herein. Polypeptide

SSC, 0.5% SDS, 1.0 mM EDTA (pH 8.0); hybridizing at 50°C-65°C, 5X SSC, overnight or, in the event of cross-species homology, at 45°C with 0.5X SSC; followed by washing twice at 65°C for 20 minutes with each of 2X, 0.5X and 0.2X SSC containing 0.1% SDS. Such hybridizing DNA sequences are also within the scope of this invention, as are nucleotide sequences that, due to code degeneracy, encode an immunogenic polypeptide that is encoded by a hybridizing DNA sequence.

Two nucleotide or polypeptide sequences are said to be "identical" if the sequence of nucleotides or amino acid residues in the two sequences is the same when aligned for maximum correspondence as described below. Comparisons between two sequences are typically performed by comparing the sequences over a comparison window to identify and compare local regions of sequence similarity. A "comparison window" as used herein, refers to a segment of at least about 20 contiguous positions, usually 30 to about 75, 40 to about 50, in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned.

Optimal alignment of sequences for comparison may be conducted using the Megalign program in the Lasergene suite of bioinformatics software (DNASTAR, Inc., Madison, WI), using default parameters. This program embodies several alignment schemes described in the following references: Dayhoff, M.O. (1978) A model of evolutionary change in proteins - Matrices for detecting distant relationships. In Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure, National Biomedical Research Foundation, Washington DC Vol. 5, Suppl. 3, pp. 345-358; Hein J. (1990) Unified Approach to Alignment and Phylogenies pp. 626-645 *Methods in Enzymology* vol. 183, Academic Press, Inc., San Diego, CA; Higgins, D.G. and Sharp, P.M. (1989) Fast and sensitive multiple sequence alignments on a microcomputer *CABIOS* 5:151-153; Myers, E.W. and Muller W. (1988) Optimal alignments in linear space *CABIOS* 4:11-17; Robinson, E.D. (1971) *Comb. Theor* 11:105; Santou, N. Nes, M. (1987) The neighbor joining method. A new method for reconstructing phylogenetic trees *Mol. Biol. Evol.* 4:406-425; Sneath, P.H.A. and Sokal, R.R. (1973) *Numerical Taxonomy - the Principles and Practice of Numerical Taxonomy*, Freeman Press, San Francisco, CA; Wilbur, W.J. and Lipman, D.J. (1983) Rapid similarity searches of nucleic acid and protein data banks *Proc. Natl. Acad. Sci. USA* 80:726-730.

libraries prepared from SCID mice with mouse anti-tumor sera, as described below in Example 4. Examples of cDNA sequences that may be isolated using this technique are provided in SEQ ID NO: 149-181.

A gene encoding a polypeptide described herein (or a portion thereof) may, alternatively, be amplified from human genomic DNA, or from lung tumor cDNA, via polymerase chain reaction. For this approach, sequence-specific primers may be designed based on the nucleotide sequences provided herein and may be purchased or synthesized. An amplified portion of a specific nucleotide sequence may then be used to isolate the full length gene from a human genomic DNA library or from a lung tumor cDNA library, using well known techniques, such as those described in Sambrook et al., *Molecular Cloning: A Laboratory Manual*, Cold Spring Harbor Laboratories, Cold Spring Harbor, NY (1989).

Once a DNA sequence encoding a polypeptide is obtained, the polypeptide may be produced recombinantly by inserting the DNA sequence into an expression vector and expressing the polypeptide in an appropriate host. Any of a variety of expression vectors known to those of ordinary skill in the art may be employed to express recombinant polypeptides of this invention. Expression may be achieved in any appropriate host cell that has been transformed or transfected with an expression vector containing a polynucleotide that encodes the recombinant polypeptide. Suitable host cells include prokaryotes, yeast and higher eukaryotic cells. Preferably, the host cells employed are *E. coli*, yeast or a mammalian cell line, such as COS or CHO cells. The DNA sequences expressed in this manner may encode naturally occurring polypeptides, portions of naturally occurring polypeptides, or other variants thereof. Supernatants from suitable host/vector systems which secrete the recombinant polypeptide may be first concentrated using a commercially available filter. The concentrate may then be applied to a suitable purification matrix, such as an affinity matrix or ion exchange resin. Finally, one or more reverse phase HPLC steps can be employed to further purify the recombinant polypeptide.

Such techniques may also be used to prepare polypeptides comprising portions or variants of the native polypeptides. Portions and other variants having fewer than about 100 amino acids, and generally fewer than about 50 amino acids, may be generated using techniques well known to those of ordinary skill in the art. For example, such polypeptides may be synthesized using any of the commercially available solid-phase techniques, such as

extended conformation; (2) their inability to adopt a secondary structure that could interact with functional epitopes on the first and second polypeptides; and (3) the lack of hydrophobic or charged residues that might react with the polypeptide functional epitopes. Preferred peptide linker sequences contain Gly, Asn and Ser residues. Other near neutral amino acids, such as Thr and Ala may also be used in the linker sequence. Amino acid sequences which may be usefully employed as linkers include those disclosed in Maratea et al., *Gene* 40:39-46, 1985; Murphy et al., *Proc. Natl. Acad. Sci. USA* 83:8258-8262, 1986; U.S. Patent No. 4,935,233 and U.S. Patent No. 4,751,180. The linker sequence may be from 1 to about 50 amino acids in length. Peptide sequences are not required when the first and second polypeptides have non-essential N-terminal amino acid regions that can be used to separate the functional domains and prevent steric interference.

The ligated DNA sequences are operably linked to suitable transcriptional or translational regulatory elements. The regulatory elements responsible for expression of DNA are located only 5' to the DNA sequence encoding the first polypeptides. Similarly, stop codons require to end translation and transcription termination signals are only present 3' to the DNA sequence encoding the second polypeptide.

Fusion proteins are also provided that comprise a polypeptide of the present invention together with an unrelated immunogenic protein. Preferably the immunogenic protein is capable of eliciting a recall response. Examples of such proteins include tetanus, tuberculosis and hepatitis proteins (see, for example, Stoute et al. *New Engl. J. Med.*, 336:86-91 (1997)).

Polypeptides that comprise an immunogenic portion of a lung tumor protein may generally be used for therapy of lung cancer, wherein the polypeptide stimulates the patient's own immune response to lung tumor cells. The present invention thus provides methods for using one or more of the compounds described herein (which may be polypeptides, polynucleotides or fusion proteins) for immunotherapy of lung cancer in a patient. As used herein, a "patient" refers to any warm-blooded animal, preferably a human. A patient may be afflicted with disease, or may be free of detectable disease. Accordingly, the compounds disclosed herein may be used to treat lung cancer or to inhibit the development of lung cancer. In a preferred embodiment, the compounds are administered

ordinary skill in the art. The DNA may also be "naked," as described, for example, in published PCT application WO 90/11092, and Ulmer et al., *Science* 259:1745-1749, 1993, reviewed by Cohen, *Science* 259:1691-1692, 1993. The uptake of naked DNA may be increased by coating the DNA onto biodegradable beads, which are efficiently transported  
5 into the cells.

Routes and frequency of administration, as well as dosage, will vary from individual to individual and may parallel those currently being used in immunotherapy of other diseases. In general, the pharmaceutical compositions and vaccines may be administered by injection (e.g., intracutaneous, intramuscular, intravenous or subcutaneous),  
10 intranasally (e.g., by aspiration) or orally. Between 1 and 10 doses may be administered over a 3-24 week period. Preferably, 4 doses are administered, at an interval of 3 months, and booster administrations may be given periodically thereafter. Alternate protocols may be appropriate for individual patients. A suitable dose is an amount of polypeptide or DNA that is effective to raise an immune response (cellular and/or humoral) against lung tumor cells in  
15 a treated patient. A suitable immune response is at least 10-50% above the basal (i.e., untreated) level. In general, the amount of polypeptide present in a dose (or produced *in situ* by the DNA in a dose) ranges from about 1 pg to about 100 mg per kg of host, typically from about 10 pg to about 1 mg, and preferably from about 100 pg to about 1 µg. Suitable dose sizes will vary with the size of the patient, but will typically range from about 0.01 mL to  
20 about 5 mL.

While any suitable carrier known to those of ordinary skill in the art may be employed in the pharmaceutical compositions of this invention, the type of carrier will vary depending on the mode of administration. For parenteral administration, such as subcutaneous injection, the carrier preferably comprises water, saline, alcohol, a lipid, a wax  
25 and/or a buffer. For oral administration, any of the above carriers or a solid carrier, such as mannitol, lactose, starch, magnesium stearate, sodium saccharine, talcum, cellulose, glucose, sucrose, and/or magnesium carbonate, may be employed. Biodegradable microspheres (e.g., polylactic glycolide) may also be employed as carriers for the pharmaceutical compositions of this invention. Suitable biodegradable microspheres are disclosed, for example, in U.S.  
30 Patent Nos. 4,897,268 and 5,075,109.



(Natural Killer cells, lymphokine-activated killer cells), B cells, or antigen presenting cells (such as dendritic cells and macrophages) expressing the disclosed antigens. The polypeptides disclosed herein may also be used to generate antibodies or anti-idiotypic antibodies (as in U.S. Patent No. 4,918,164), for passive immunotherapy.

5 The predominant method of procuring adequate numbers of T-cells for adoptive immunotherapy is to grow immune T-cells *in vitro*. Culture conditions for expanding single antigen-specific T-cells to several billion in number with retention of antigen recognition *in vivo* are well known in the art. These *in vitro* culture conditions typically utilize intermittent stimulation with antigen, often in the presence of cytokines, such  
10 as IL-2, and non-dividing feeder cells. As noted above, the immunoreactive polypeptides described herein may be used to rapidly expand antigen-specific T cell cultures in order to generate sufficient number of cells for immunotherapy. In particular, antigen-presenting cells, such as dendritic, macrophage or B-cells, may be pulsed with immunoreactive polypeptides or transfected with a polynucleotide sequence(s), using standard techniques well  
15 known in the art. For cultured T-cells to be effective in therapy, the cultured T-cells must be able to grow and distribute widely and to survive long term *in vivo*. Studies have demonstrated that cultured T-cells can be induced to grow *in vivo* and to survive long term in substantial numbers by repeated stimulation with antigen supplemented with IL-2 (see, for example, Cheever et al. *Ibid*).

20 The polypeptides disclosed herein may also be employed to generate and/or isolate tumor-reactive T-cells, which can then be administered to the patient. In one technique, antigen-specific T-cell lines may be generated by *in vivo* immunization with short peptides corresponding to immunogenic portions of the disclosed polypeptides. The resulting antigen specific CD8+ CTL clones may be isolated from the patient, expanded using standard  
25 tissue culture techniques, and returned to the patient.

Alternatively, peptides corresponding to immunogenic portions of the polypeptides may be employed to generate tumor reactive T cell subsets by selective *in vitro* stimulation and expansion of autologous T cells to provide antigen-specific T cells which may be subsequently transferred to the patient as described, for example, by Chang et al.  
30 (*Crit. Rev. Oncol. Hematol.*, 22(3), 213, 1996).

at least about 80%, and preferably at least about 90%) of the patients for which lung cancer would be indicated using the full length protein, and that indicate the absence of lung cancer in substantially all of those samples that would be negative when tested with full length protein. The representative assays described below, such as the two-antibody sandwich  
5 assay, may generally be employed for evaluating the ability of a binding agent to detect metastatic human lung tumors.

The ability of a polypeptide prepared as described herein to generate antibodies capable of detecting primary or metastatic human lung tumors may generally be evaluated by raising one or more antibodies against the polypeptide (using, for example, a  
10 representative method described herein) and determining the ability of such antibodies to detect such tumors in patients. This determination may be made by assaying biological samples from patients with and without primary or metastatic lung cancer for the presence of a polypeptide that binds to the generated antibodies. Such test assays may be performed, for example, using a representative procedure described below. Polypeptides that generate  
15 antibodies capable of detecting at least 20% of primary or metastatic lung tumors by such procedures are considered to be useful in assays for detecting primary or metastatic human lung tumors. Polypeptide specific antibodies may be used alone or in combination to improve sensitivity.

Polypeptides capable of detecting primary or metastatic human lung tumors  
20 may be used as markers for diagnosing lung cancer or for monitoring disease progression in patients. In one embodiment, lung cancer in a patient may be diagnosed by evaluating a biological sample obtained from the patient for the level of one or more of the above polypeptides, relative to a predetermined cut-off value. As used herein, suitable "biological samples" include blood, sera, urine and/or lung secretions.

25 The level of one or more of the above polypeptides may be evaluated using any binding agent specific for the polypeptide(s). A "binding agent," in the context of this invention, is any agent (such as a compound or a cell) that binds to a polypeptide as described above. As used herein, "binding" refers to a noncovalent association between two separate molecules (each of which may be free (*i.e.*, in solution) or present on the surface of a cell or a  
30 solid support), such that a "complex" is formed. Such a complex may be free or immobilized (either covalently or noncovalently) on a support material. The ability to bind may generally

be immobilized on the solid support using a variety of techniques known to those of skill in the art, which are amply described in the patent and scientific literature. In the context of the present invention, the term "immobilization" refers to both noncovalent association, such as adsorption, and covalent attachment (which may be a direct linkage between the antigen and functional groups on the support or may be a linkage by way of a cross-linking agent).  
5 Immobilization by adsorption to a well in a microtiter plate or to a membrane is preferred. In such cases, adsorption may be achieved by contacting the binding agent, in a suitable buffer, with the solid support for a suitable amount of time. The contact time varies with temperature, but is typically between about 1 hour and about 1 day. In general, contacting a  
10 well of a plastic microtiter plate (such as polystyrene or polyvinylchloride) with an amount of binding agent ranging from about 10 ng to about 10  $\mu$ g, and preferably about 100 ng to about 1  $\mu$ g, is sufficient to immobilize an adequate amount of binding agent.

Covalent attachment of binding agent to a solid support may generally be achieved by first reacting the support with a bifunctional reagent that will react with both the  
15 support and a functional group, such as a hydroxyl or amino group, on the binding agent. For example, the binding agent may be covalently attached to supports having an appropriate polymer coating using benzoquinone or by condensation of an aldehyde group on the support with an amine and an active hydrogen on the binding partner (*see, e.g.,* Pierce Immunotechnology Catalog and Handbook, 1991, at A12-A13).

20 In certain embodiments, the assay is a two-antibody sandwich assay. This assay may be performed by first contacting an antibody that has been immobilized on a solid support, commonly the well of a microtiter plate, with the sample, such that polypeptides within the sample are allowed to bind to the immobilized antibody. Unbound sample is then removed from the immobilized polypeptide-antibody complexes and a second antibody  
25 (containing a reporter group) capable of binding to a different site on the polypeptide is added. The amount of second antibody that remains bound to the solid support is then determined using a method appropriate for the specific reporter group.

More specifically, once the antibody is immobilized on the support as described above, the remaining protein binding sites on the support are typically blocked.  
30 Any suitable blocking agent known to those of ordinary skill in the art, such as bovine serum albumin or Tween 20™ (Sigma Chemical Co., St. Louis, MO). The immobilized antibody is

that corresponds to a predetermined cut-off value. In one preferred embodiment, the cut-off value is the average mean signal obtained when the immobilized antibody is incubated with samples from patients without lung cancer. In general, a sample generating a signal that is three standard deviations above the predetermined cut-off value is considered positive for lung cancer. In an alternate preferred embodiment, the cut-off value is determined using a Receiver Operator Curve, according to the method of Sackett et al., *Clinical Epidemiology: A Basic Science for Clinical Medicine*, Little Brown and Co., 1985, p. 106-7. Briefly, in this embodiment, the cut-off value may be determined from a plot of pairs of true positive rates (i.e., sensitivity) and false positive rates (100%-specificity) that correspond to each possible cut-off value for the diagnostic test result. The cut-off value on the plot that is the closest to the upper left-hand corner (i.e., the value that encloses the largest area) is the most accurate cut-off value, and a sample generating a signal that is higher than the cut-off value determined by this method may be considered positive. Alternatively, the cut-off value may be shifted to the left along the plot, to minimize the false positive rate, or to the right, to minimize the false negative rate. In general, a sample generating a signal that is higher than the cut-off value determined by this method is considered positive for lung cancer.

In a related embodiment, the assay is performed in a flow-through or strip test format, wherein the antibody is immobilized on a membrane, such as nitrocellulose. In the flow-through test, polypeptides within the sample bind to the immobilized antibody as the sample passes through the membrane. A second, labeled antibody then binds to the antibody-polypeptide complex as a solution containing the second antibody flows through the membrane. The detection of bound second antibody may then be performed as described above. In the strip test format, one end of the membrane to which antibody is bound is immersed in a solution containing the sample. The sample migrates along the membrane through a region containing second antibody and to the area of immobilized antibody. Concentration of second antibody at the area of immobilized antibody indicates the presence of lung cancer. Typically, the concentration of second antibody at that site generates a pattern, such as a line, that can be read visually. The absence of such a pattern indicates a negative result. In general, the amount of antibody immobilized on the membrane is selected to generate a visually discernible pattern when the biological sample contains a level of polypeptide that would be sufficient to generate a positive signal in the two-antibody

of immortal cell lines capable of producing antibodies having the desired specificity (*i.e.*, reactivity with the polypeptide of interest). Such cell lines may be produced, for example, from spleen cells obtained from an animal immunized as described above. The spleen cells are then immortalized by, for example, fusion with a myeloma cell fusion partner, preferably one that is syngeneic with the immunized animal. A variety of fusion techniques may be employed. For example, the spleen cells and myeloma cells may be combined with a nonionic detergent for a few minutes and then plated at low density on a selective medium that supports the growth of hybrid cells, but not myeloma cells. A preferred selection technique uses HAT (hypoxanthine, aminopterin, thymidine) selection. After a sufficient time, usually about 1 to 2 weeks, colonies of hybrids are observed. Single colonies are selected and tested for binding activity against the polypeptide. Hybridomas having high reactivity and specificity are preferred.

Monoclonal antibodies may be isolated from the supernatants of growing hybridoma colonies. In addition, various techniques may be employed to enhance the yield, such as injection of the hybridoma cell line into the peritoneal cavity of a suitable vertebrate host, such as a mouse. Monoclonal antibodies may then be harvested from the ascites fluid or the blood. Contaminants may be removed from the antibodies by conventional techniques, such as chromatography, gel filtration, precipitation, and extraction. The polypeptides of this invention may be used in the purification process in, for example, an affinity chromatography step.

Monoclonal antibodies of the present invention may also be used as therapeutic reagents, to diminish or eliminate lung tumors. The antibodies may be used on their own (for instance, to inhibit metastases) or coupled to one or more therapeutic agents. Suitable agents in this regard include radionuclides, differentiation inducers, drugs, toxins, and derivatives thereof. Preferred radionuclides include  $^{90}\text{Y}$ ,  $^{123}\text{I}$ ,  $^{125}\text{I}$ ,  $^{131}\text{I}$ ,  $^{186}\text{Re}$ ,  $^{188}\text{Re}$ ,  $^{211}\text{At}$ , and  $^{212}\text{Bi}$ . Preferred drugs include methotrexate, and pyrimidine and purine analogs. Preferred differentiation inducers include phorbol esters and butyric acid. Preferred toxins include ricin, abrin, diphtheria toxin, cholera toxin, gelonin, *Pseudomonas* exotoxin, *Shigella* toxin, and pokeweed antiviral protein.

A therapeutic agent may be coupled (*e.g.*, covalently bonded) to a suitable monoclonal antibody either directly or indirectly (*e.g.*, via a linker group). A direct reaction

be prepared in a variety of ways. For example, more than one agent may be coupled directly to an antibody molecule, or linkers which provide multiple sites for attachment can be used. Alternatively, a carrier can be used.

A carrier may bear the agents in a variety of ways, including covalent bonding either directly or via a linker group. Suitable carriers include proteins such as albumins (e.g., U.S. Patent No. 4,507,234, to Kato et al.), peptides and polysaccharides such as aminodextran (e.g., U.S. Patent No. 4,699,784, to Shih et al.). A carrier may also bear an agent by noncovalent bonding or by encapsulation, such as within a liposome vesicle (e.g., U.S. Patent Nos. 4,429,008 and 4,873,088). Carriers specific for radionuclide agents include radiohalogenated small molecules and chelating compounds. For example, U.S. Patent No. 4,735,792 discloses representative radiohalogenated small molecules and their synthesis. A radionuclide chelate may be formed from chelating compounds that include those containing nitrogen and sulfur atoms as the donor atoms for binding the metal, or metal oxide, radionuclide. For example, U.S. Patent No. 4,673,562, to Davison et al. discloses representative chelating compounds and their synthesis.

A variety of routes of administration for the antibodies and immunoconjugates may be used. Typically, administration will be intravenous, intramuscular, subcutaneous or in the bed of a resected tumor. It will be evident that the precise dose of the antibody/immunoconjugate will vary depending upon the antibody used, the antigen density on the tumor, and the rate of clearance of the antibody.

Diagnostic reagents of the present invention may also comprise DNA sequences encoding one or more of the above polypeptides, or one or more portions thereof. For example, at least two oligonucleotide primers may be employed in a polymerase chain reaction (PCR) based assay to amplify lung tumor-specific cDNA derived from a biological sample, wherein at least one of the oligonucleotide primers is specific for a polynucleotide encoding a lung tumor protein of the present invention. The presence of the amplified cDNA is then detected using techniques well known in the art, such as gel electrophoresis. Similarly, oligonucleotide probes specific for a polynucleotide encoding a lung tumor protein of the present invention may be used in a hybridization assay to detect the presence of an inventive polypeptide in a biological sample.

The following Examples are offered by way of illustration and not by way of limitation.

### EXAMPLES

#### Example 1

#### PREPARATION OF LUNG TUMOR-SPECIFIC cDNA SEQUENCES USING DIFFERENTIAL DISPLAY RT-PCR

This example illustrates the preparation of cDNA molecules encoding lung tumor-specific polypeptides using a differential display screen.

Tissue samples were prepared from breast tumor and normal tissue of a patient with lung cancer that was confirmed by pathology after removal of samples from the patient. Normal RNA and tumor RNA was extracted from the samples and mRNA was isolated and converted into cDNA using a (dT)<sub>12</sub>AG (SEQ ID NO: 47) anchored 3' primer. Differential display PCR was then executed using a randomly chosen primer (SEQ ID NO: 48). Amplification conditions were standard buffer containing 1.5 mM MgCl<sub>2</sub>, 20 pmol of primer, 500 pmol dNTP and 1 unit of Taq DNA polymerase (Perkin-Elmer, Branchburg, NJ). Forty cycles of amplification were performed using 94 °C denaturation for 30 seconds, 42 °C annealing for 1 minute and 72 °C extension for 30 seconds. Bands that were repeatedly observed to be specific to the RNA fingerprint pattern of the tumor were cut out of a silver stained gel, subcloned into the pGEM-T vector (Promega, Madison, WI) and sequenced. The isolated 3' sequences are provided in SEQ ID NO: 1-16.

Comparison of these sequences to those in the public databases using the BLASTN program, revealed no significant homologies to the sequences provided in SEQ ID NO: 1-11. To the best of the inventors' knowledge, none of the isolated DNA sequences have previously been shown to be expressed at a greater level in human lung tumor tissue than in normal lung tissue.

aminopeptidase. Clone LT86-9 appears to contain two inserts, with the 5' sequence showing homology to the previously identified antisense sequence of interferon alpha-induced P27, and the 3' sequence being similar to LT86-6. Clone LT86-14 (SEQ ID NO: 30) was found to show some homology to the trithorax gene and has an "RGD" cell attachment sequence and a  
5 beta-Lactamase A site which functions in hydrolysis of penicillin. Clones LT86-1, LT86-2, LT86-4, LT86-5 and LT86-10 (SEQ ID NOS: 17, 18; 20, 21 and 26, respectively) were found to show homology to previously identified genes. A subsequently determined extended cDNA sequence for LT86-4 is provided in SEQ ID NO: 66, with the corresponding predicted amino acid sequence being provided in SEQ ID NO: 67.

10 Subsequent studies led to the isolation of five additional clones, referred to as LT86-20, LT86-21, LT86-22, LT86-26 and LT86-27. The determined 5' cDNA sequences for LT86-20, LT86-22, LT86-26 and LT86-27 are provided in SEQ ID NO: 68 and 70-72, respectively, with the determined 3' cDNA sequences for LT86-21 being provided in SEQ ID  
15 NO: 69. The corresponding predicted amino acid sequences for LT86-20, LT86-21, LT86-22, LT86-26 and LT86-27 are provided in SEQ ID NO: 73-77, respectively. LT86-22 and LT86-27 were found to be highly similar to each other. Comparison of these sequences to those in the gene bank as described above, revealed no significant homologies to LT86-22 and LT86-27. LT86-20, LT86-21 and LT86-26 were found to show homology to previously  
20 identified genes.



predicted amino acid sequences are provided in SEQ ID NO: 93-101, respectively. L86S-30, L86S-39 and L86S-47 were found to be similar to each other. Comparison of these sequences with those in the gene bank as described above, revealed no significant homologies to L86S-14. L86S-29 was found to show some homology to a previously identified EST. 5 L86S-6, L86S-11, L86S-34, L86S-39, L86S-47, L86S-49 and L86S-51 were found to show some homology to previously identified genes.

In further studies, a directional cDNA library was constructed using a Stratagene kit with a Lambda Zap Express vector. Total RNA for the library was isolated from two primary squamous lung tumors and poly A+ RNA was isolated using an oligo dT 10 column. Antiserum was developed in normal mice using a pool of sera from three SCID mice implanted with human squamous lung carcinomas. Approximately 700,000 PFUs were screened from the unamplified library with *E. coli* absorbed mouse anti-SCID tumor serum. Positive plaques were identified as described above. Phage was purified and phagemid excised for 180 clones with inserts in a pBK-CMV vector for expression in prokaryotic or 15 eukaryotic cells.

The determined cDNA sequences for 23 of the isolated clones are provided in SEQ ID NO: 126-148. Comparison of these sequences with those in the public database as described above revealed no significant homologies to the sequences of SEQ ID NO: 139 and 143-148. The sequences of SEQ ID NO: 126-138 and 140-142 were found to show 20 homology previously identified human polynucleotide sequences.

tags (ESTs). The sequences of SEQ ID NO: 150, 155 and 159-181 were found to show homology to sequences previously identified in humans.

Example 6

## ISOLATION OF DNA SEQUENCES ENCODING LUNG TUMOR ANTIGENS

DNA sequences encoding antigens potentially involved in squamous cell lung  
5 tumor formation were isolated as follows.

A lung tumor directional cDNA expression library was constructed employing  
the Lambda ZAP Express expression system (Stratagene, La Jolla, CA). Total RNA for the  
library was taken from a pool of two human squamous epithelial lung carcinomas and poly  
A+ RNA was isolated using oligo-dT cellulose (Gibco BRL, Gaithersburg, MD). Phagemid  
10 were rescued at random and the cDNA sequences of isolated clones were determined.

The determined cDNA sequence for the clone SLT-T1 is provided in SEQ ID  
NO: 102, with the determined 5' cDNA sequences for the clones SLT-T2, SLT-T3, SLT-T5,  
SLT-T7, SLT-T9, SLT-T10, SLT-T11 and SLT-T12 being provided in SEQ ID NO: 103-  
110, respectively. The corresponding predicted amino acid sequence for SLT-T1, SLT-T2,  
15 SLT-T3, SLT-T10 and SLT-T12 are provided in SEQ ID NO: 111-115, respectively.  
Comparison of the sequences for SLT-T2, SLT-T3, SLT-T5, SLT-T7, SLT-T9 and SLT-T11  
with those in the public databases as described above, revealed no significant homologies.  
The sequences for SLT-T10 and SLT-T12 were found to show some homology to sequences  
previously identified in humans.

20 The sequence of SLT-T1 was determined to show some homology to a PAC  
clone of unknown protein function. The cDNA sequence of SLT-T1 (SEQ ID NO: 102) was  
found to contain a mutator (MUT) domain. Such domains are known to function in removal  
of damaged guanine from DNA that can cause A to G transversions (see, for example, el-  
Deiry, W.S., 1997 *Curr. Opin. Oncol.* 9:79-87; Okamoto, K. et al. 1996 *Int. J. Cancer*  
25 65:437-41; Wu, C. et al. 1995 *Biochem. Biophys. Res. Commun.* 214:1239-45; Porter, D.W.  
et al. 1996 *Chem. Res. Toxicol.* 9:1375-81). SLT-T1 may thus be of use in the treatment, by  
gene therapy, of lung cancers caused by, or associated with, a disruption in DNA repair.

Example 7

## SYNTHESIS OF POLYPEPTIDES

Polypeptides may be synthesized on a Perkin Elmer/Applied Biosystems  
5 Division 430A peptide synthesizer using Fmoc chemistry with HPTU (O-Benzotriazole-  
N,N,N',N'-tetramethyluronium hexafluorophosphate) activation. A Gly-Cys-Gly sequence  
may be attached to the amino terminus of the peptide to provide a method of conjugation,  
binding to an immobilized surface, or labeling of the peptide. Cleavage of the peptides from  
the solid support may be carried out using the following cleavage mixture: trifluoroacetic  
10 acid:ethanedithiol:thioanisole:water:phenol (40:1:2:2:3). After cleaving for 2 hours, the  
peptides may be precipitated in cold methyl-t-butyl-ether. The peptide pellets may then be  
dissolved in water containing 0.1% trifluoroacetic acid (TFA) and lyophilized prior to  
purification by C18 reverse phase HPLC. A gradient of 0%-60% acetonitrile (containing  
0.1% TFA) in water (containing 0.1% TFA) may be used to elute the peptides. Following  
15 lyophilization of the pure fractions, the peptides may be characterized using electrospray or  
other types of mass spectrometry and by amino acid analysis.

From the foregoing, it will be appreciated that, although specific embodiments  
of the invention have been described herein for the purposes of illustration, various  
20 modifications may be made without deviating from the spirit and scope of the invention.

9. A vaccine comprising the polypeptide of claim 2 and an immune response enhancer.

5 10. The vaccine of claim 9 wherein the immune response enhancer is an adjuvant.

11. A vaccine comprising the polynucleotide of claims 1 or 4 and an immune response enhancer.

10

12. The vaccine of claim 11 wherein the immune response enhancer is an adjuvant.

13. A pharmaceutical composition for the treatment of lung cancer  
15 comprising a polypeptide and a physiologically acceptable carrier, the polypeptide comprising an immunogenic portion of a lung protein or of a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide comprising a sequence selected from the group consisting of:

(a) sequences recited in SEQ ID NO: 12-18, 20, 21, 26, 49, 50, 52, 54, 64,  
20 66, 68, 69, 71, 78, 84, 85, 88, 91, 92, 116-120, 126-138, 140-142, 150, 155 and 159-181;

(b) sequences complementary to the sequences of SEQ ID NO: 12-18, 20,  
21, 26, 49, 50, 52, 54, 64, 66, 68, 69, 71, 78, 84, 85, 88, 91, 92, 116-120, 126-138, 140-142,  
150, 155 and 159-181; and

(c) variants of the sequences of (a) and (b).

25

14. A vaccine for the treatment of lung cancer comprising a polypeptide and an immune response enhancer, said polypeptide comprising an immunogenic portion of a lung protein or of a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide comprising a sequence selected from the group consisting of:

30 (a) sequences recited in SEQ ID NO: 12-18, 20, 21, 26, 49, 50, 52, 54, 64,  
66, 68, 69, 71, 78, 84, 85, 88, 91, 92, 116-120, 126-138, 140-142, 150, 155 and 159-181;

21. A pharmaceutical composition comprising a fusion protein according to any one of claims 18-20 and a physiologically acceptable carrier.

5 22. A vaccine comprising a fusion protein according to any one of claims 18-20 and an immune response enhancer.

23. The vaccine of claim 22 wherein the immune response enhancer is an adjuvant.

10

24. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient an effective amount of the pharmaceutical composition of claim 21.

15

25. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient an effective amount of the vaccine of claim 22.

26. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient a polynucleotide under conditions such that the polynucleotide enters a cell of the patient and is expressed therein, the polynucleotide having a sequence selected from the group consisting of:

20

- (a) a sequence provided in SEQ ID NO: 102;
- (b) sequences complementary to a sequence of SEQ ID NO: 102; and
- (c) variants of the sequence of SEQ ID NO: 102.

25

27. A method for detecting lung cancer in a patient, comprising:

- (a) contacting a biological sample obtained from the patient with a binding agent which is capable of binding to a polypeptide, the polypeptide comprising an immunogenic portion of a lung tumor protein or a variant thereof, wherein said protein comprises an amino acid sequence encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of sequences provided in SEQ ID NO: 1-31, 49-

30

- (a) sequences recited in SEQ ID NO: 1-11, 19, 22-25, 27-31, 51, 53, 55, 63, 70, 72, 79, 80, 86, 87, 89, 90, 102-107, 109, 139, 143-149, 151-154 and 156-158;
- (b) the complements of nucleotide sequences recited in SEQ ID NO: 1-11, 19, 22-25, 27-31, 51, 53, 55, 63, 70, 72, 79, 80, 86, 87, 89, 90, 102-107, 109, 139, 143-149, 151-154 and 156-158; and
- (c) variants of the sequences of (a) and (b).

32. A method for inhibiting the development of lung cancer in a patient, comprising administering to the patient a therapeutically effective amount of a monoclonal antibody according to claim 31.

33. The method of claim 32 wherein the monoclonal antibody is conjugated to a therapeutic agent.

34. A method for detecting lung cancer in a patient comprising:

- (a) obtaining a biological sample from the patient;
- (b) contacting the sample with at least two oligonucleotide primers in a polymerase chain reaction, wherein at least one of the oligonucleotides is specific for a polynucleotide encoding a polypeptide comprising an immunogenic portion of a lung tumor protein or a variant thereof, said protein comprising an amino acid sequence encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of sequences recited in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said sequences and variants thereof; and
- (c) detecting in the sample a DNA sequence that amplifies in the presence of the oligonucleotide primers, thereby detecting lung cancer.

35. The method of claim 34, wherein at least one of the oligonucleotide primers comprises at least about 10 contiguous nucleotides of a polynucleotide comprising a sequence selected from SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181.

provided in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said sequences and variants thereof.

44. A method for detecting lung cancer in a patient, comprising:

(a) obtaining a biological sample from the patient;

5 (b) contacting the biological sample with an oligonucleotide probe specific for a polynucleotide encoding a polypeptide comprising an immunogenic portion of a lung tumor protein or a variant thereof, said protein comprising an amino acid sequence encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of sequences recited in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said nucleotide sequences and variants thereof; and

10 (c) detecting in the sample a DNA sequence that hybridizes to the oligonucleotide probe, thereby detecting lung cancer in the patient.

45. The method of claim 44 wherein the oligonucleotide probe comprises at least about 15 contiguous nucleotides of a polynucleotide having a nucleotide sequence  
15 selected from the group consisting of sequences recited in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said nucleotide sequences and variants thereof.

46. A diagnostic kit comprising an oligonucleotide probe specific for a polynucleotide encoding a polypeptide comprising an immunogenic portion of a lung tumor  
20 protein or a variant thereof, said protein comprising an amino acid sequence encoded by a polynucleotide comprising a nucleotide sequence selected from the group consisting of sequences recited in SEQ ID NO: 1-31, 49-55, 63, 64, 66, 68-72, 78-80, 84-92, 102-110, 116-120 and 126-181, the complements of said sequences and variants thereof.

47. The diagnostic kit of claim 46, wherein the oligonucleotide probe  
25 comprises at least about 15 contiguous nucleotides of a polynucleotide having a nucleotide sequence selected from the group consisting of sequences recited in SEQ ID NO: 1-31, 49-55,



pharmaceutically acceptable carrier.

55. A composition for the treatment of lung cancer in a patient, comprising T cells proliferated in the presence of a polynucleotide of claim 1, in combination with a  
5 pharmaceutically acceptable carrier.

56. A method for treating lung cancer in a patient, comprising the steps of:
- (a) incubating antigen presenting cells in the presence of at least one polypeptide of claim 2; and  
10 (b) administering to the patient the incubated antigen presenting cells.

57. A method for treating lung cancer in a patient, comprising the steps of:
- (a) incubating antigen presenting cells in the presence of at least one polynucleotide of claim 1; and  
15 (b) administering to the patient the incubated antigen presenting cells.

58. The method of claims 54 or 55 wherein the antigen presenting cells are selected from the group consisting of dendritic cells and macrophage cells.

- 20 59. A composition for the treatment of lung cancer in a patient, comprising antigen presenting cells incubated in the presence of a polypeptide of claim 2, in combination with a pharmaceutically acceptable carrier.

60. A composition for the treatment of lung cancer in a patient, comprising  
25 antigen presenting cells incubated in the presence of a polynucleotide of claim 1, in combination with a pharmaceutically acceptable carrier.

## SEQUENCE LISTING

&lt;110&gt; Corixa Corporation

&lt;120&gt; COMPOUNDS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER AND METHODS FOR THEIR USE

&lt;130&gt; 210121.447PC

&lt;140&gt; PCT

&lt;141&gt; 1999-01-28

&lt;160&gt; 216

&lt;170&gt; PatentIn Ver. 2.0

&lt;210&gt; 1

&lt;211&gt; 339

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 1

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&lt;212&gt; DNA

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&lt;211&gt; 697

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 3

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&lt;210&gt; 4

&lt;211&gt; 712

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 4

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wtttyccsc cygsykggct gggasckgtt myyyyygntm csyagcttgc tt 712

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&lt;210&gt; 5

&lt;211&gt; 679

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 5

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tccggaanct tggtttccc 679

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&lt;210&gt; 6

&lt;211&gt; 369

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

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<210> 7  
<211> 264  
<212> DNA  
<213> Homo sapiens

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ttcttctcac tgagtcaccc agca 264

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<211> 280  
<212> DNA  
<213> Homo sapiens

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<211> 449  
<212> DNA  
<213> Homo sapiens

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<212> DNA  
<213> Homo sapiens

<400> 10  
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&lt;210&gt; 11

&lt;211&gt; 543

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 11

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tcaggcatct gggacttgat gtgggnttgg gatttgaat cagagcacct nggtctctst 180  
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aaa 543

&lt;210&gt; 12

&lt;211&gt; 329

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 12

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gagccacaga gtcaaataaa aatcaatttt gagagaccac agcacctgct gctttgatcg 300  
tgatgttcaa ggcaagttgc aagtcacg 329

&lt;210&gt; 13

&lt;211&gt; 314

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 13

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&lt;210&gt; 14

&lt;211&gt; 691

&lt;212&gt; DNA

<213> Homo sapiens

<400> 14

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<210> 15

<211> 355

<212> DNA

<213> Homo sapiens

<400> 15

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<210> 16

<211> 522

<212> DNA

<213> Homo sapiens

<400> 16

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<210> 17

<211> 317

<212> DNA

<213> Homo sapiens

<400> 17

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<210> 18

<211> 392

<212> DNA

<213> Homo sapiens

<400> 18

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<210> 19

<211> 2624

<212> DNA

<213> Homo sapiens

<400> 19

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&lt;210&gt; 20

&lt;211&gt; 488

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 20

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cctaacc 488

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&lt;210&gt; 21

&lt;211&gt; 391

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 21

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ctgaagatct agaagatgct ctgaagagca g 391

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&lt;210&gt; 22

&lt;211&gt; 1320

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 22

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&lt;210&gt; 23

&lt;211&gt; 633

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 23

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&lt;210&gt; 24

&lt;211&gt; 1328

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 24

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&lt;210&gt; 25

&lt;211&gt; 1758

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 25

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&lt;210&gt; 26

&lt;211&gt; 493

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 26

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<210> 27

<211> 1331

<212> DNA

<213> Homo sapiens

<400> 27

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<210> 28

<211> 1333

<212> DNA

<213> Homo sapiens

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1333

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<210> 29  
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 <212> DNA  
 <213> Homo sapiens

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 <211> 1316  
 <212> DNA  
 <213> Homo sapiens

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 <211> 1355  
 <212> DNA  
 <213> Homo sapiens

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<210> 32  
 <211> 80  
 <212> PRT  
 <213> Homo sapiens

<400> 32  
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 Val Leu Lys Tyr Tyr Lys Val Asp Glu Asn Gly Lys Ile Ser Cys Leu  
 35 40 45  
 Arg Arg Glu Cys Pro Ser Asp Glu Cys Gly Ala Gly Val Phe Met Ala  
 50 55 60

Ser His Phe Asp Arg His Tyr Cys Gly Lys Cys Cys Leu Thr His Cys  
 65 70 75 80

<210> 33  
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 <212> PRT  
 <213> Homo sapiens

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 Lys Lys His Pro Asp Phe Pro Lys Lys Pro Leu Thr Pro Tyr Phe Arg  
 35 40 45  
 Phe Phe Met Glu Lys Arg Ala Lys Tyr Ala Lys Leu His Pro Gln Met  
 50 55 60  
 Ser Asn Leu Asp Leu Thr Lys Ile Leu Ser Lys Lys Tyr Lys Glu Leu  
 65 70 75 80  
 Pro Glu Lys Lys Lys Met Lys Tyr Val Pro Asp Phe Gln Arg Arg Glu  
 85 90 95  
 Thr Gly Val Arg Ala Lys Pro Gly Pro Ile Gln Gly Gly Ser Pro Pro  
 100 105 110  
 Pro Tyr Pro Glu Cys Gln Glu Ser Asp Ile Pro Glu Lys Pro Gln Asp  
 115 120 125  
 Pro Pro  
 130

<210> 34  
 <211> 506  
 <212> PRT  
 <213> Homo sapiens

<400> 34  
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 Ser Ile Cys Met Arg Met Glu Ile Leu Gly Cys Pro Leu Pro Asp Pro

35	40	45
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50	55	60
Asp Phe Lys His His Asn Tyr Lys Glu Met Arg Gln Leu Met Lys Val		
65	70	75 80
Val Asn Glu Met Cys Pro Asn Ile Thr Arg Ile Tyr Asn Ile Gly Lys		
	85	90 95
Ser His Gln Gly Leu Lys Leu Tyr Ala Val Glu Ile Ser Asp His Pro		
	100	105 110
Gly Glu His Glu Val Gly Glu Pro Glu Phe His Tyr Ile Ala Gly Ala		
	115	120 125
His Gly Asn Glu Val Leu Gly Arg Glu Leu Leu Leu Leu Leu His		
	130	135 140
Phe Leu Cys Gln Glu Tyr Ser Ala Gln Asn Ala Arg Ile Val Arg Leu		
145	150	155 160
Val Glu Glu Thr Arg Ile His Ile Leu Pro Ser Leu Asn Pro Asp Gly		
	165	170 175
Tyr Glu Lys Ala Tyr Glu Gly Gly Ser Glu Leu Gly Gly Trp Ser Leu		
	180	185 190
Gly Arg Trp Thr His Asp Gly Ile Asp Ile Asn Asn Asn Phe Pro Asp		
	195	200 205
Leu Asn Ser Leu Leu Trp Glu Ala Glu Asp Gln Gln Asn Ala Pro Arg		
	210	215 220
Lys Val Pro Asn His Tyr Ile Ala Ile Pro Glu Trp Phe Leu Ser Glu		
225	230	235 240
Asn Ala Thr Val Ala Thr Glu Thr Arg Ala Val Ile Ala Trp Met Glu		
	245	250 255
Lys Ile Pro Phe Val Leu Gly Gly Asn Leu Gln Gly Gly Glu Leu Val		
	260	265 270
Val Ala Tyr Pro Tyr Asp Met Val Arg Ser Leu Trp Lys Thr Gln Glu		
	275	280 285
His Thr Pro Thr Pro Asp Asp His Val Phe Arg Trp Leu Ala Tyr Ser		
	290	295 300
Tyr Ala Ser Thr His Arg Leu Met Thr Asp Ala Arg Arg Arg Val Cys		
305	310	315 320
His Thr Glu Asp Phe Gln Lys Glu Glu Gly Thr Val Asn Gly Ala Ser		
	325	330 335

Trp His Thr Val Ala Gly Ser Leu Asn Asp Phe Ser Tyr Leu His Thr  
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 Asn Cys Phe Glu Leu Ser Ile Tyr Val Gly Cys Asp Lys Tyr Pro His  
 355 360 365  
 Glu Ser Glu Leu Pro Glu Glu Trp Glu Asn Asn Arg Glu Ser Leu Ile  
 370 375 380  
 Val Phe Met Glu Gln Val His Arg Gly Ile Lys Gly Ile Val Arg Asp  
 385 390 395 400  
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 405 410 415  
 Asn His Asp Ile Arg Thr Ala Ser Asp Gly Asp Tyr Trp Arg Leu Leu  
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 435 440 445  
 Ser Thr Lys Asn Cys Met Val Gly Tyr Asp Met Gly Ala Thr Arg Cys  
 450 455 460  
 Asp Phe Thr Leu Thr Lys Thr Asn Leu Ala Arg Ile Arg Glu Ile Met  
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<210> 35  
 <211> 96  
 <212> PRT  
 <213> Homo sapiens

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 Cys Met Lys Asn Asn Leu Pro Ser Asn Asp Ser Ser Gln Phe Lys Thr  
 35 40 45  
 Thr Gln Thr His Met Asp Arg Glu Lys Val Ala Leu Lys Asp Phe Ser  
 50 55 60  
 Gly Asp Met Cys Lys Leu Lys Trp Val Glu Ile Ser Asn Glu Val Arg  
 65 70 75 80



Lys Phe Arg Thr Leu Thr Glu Leu Ile Leu Asp Thr Gln Glu His Val  
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 <213> Homo sapiens

<400> 36  
 Gly Ile Val Val Phe Ser Leu Gly Ser Met Val Ser Glu Ile Pro Glu  
 1 5 10 15

Lys Lys Ala Val Ala Ile Ala Asp Ala Leu Gly Lys Ile Pro Gln Thr  
 20 25 30

Val Leu Trp Arg Tyr Thr Gly Thr Arg Pro Ser Asn Leu Ala Asn Asn  
 35 40 45

Thr Ile Leu Val Gln Trp Leu Pro Gln Asn Asp Leu Leu Gly His Pro  
 50 55 60

Met Thr Arg Ala Phe Ile Thr His Ala Ser Ser His Gly Val Asn Glu  
 65 70 75 80

Ser Ile Cys Asn Gly Val Pro Met Val Met Ile Pro Leu Phe Gly Asp  
 85 90 95

Gln Met Asp Asn Ala Lys Arg Arg Glu Thr Lys Gly Ala Gly Val Thr  
 100 105 110

Leu Asn Val Leu Glu Met Thr Ser Glu Asp Leu Glu Asp Ala Leu Lys  
 115 120 125

Ser

<210> 37  
 <211> 238  
 <212> PRT  
 <213> Homo sapiens

<400> 37  
 Asn Leu Leu Gly Ile Ser Trp Val Asp Ser Ser Trp Ile Pro Ile Leu  
 1 5 10 15

Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser Glu Arg Ser Asn Pro Phe  
 20 25 30

Tyr Asp Arg Thr Cys Asn Asn Glu Val Val Lys Met Gln Arg Leu Thr  
 35 40 45

Leu Glu His Leu Asn Gln Met Val Gly Ile Glu Tyr Ile Leu Leu His  
 50 55 60

Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg Lys Gln Gln Arg Gln Ser  
 65 70 75 80  
 Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr Tyr Ile Ile Ala Gly Val  
 85 90 95  
 Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val Ile Asn Ser Arg Val Leu  
 100 105 110  
 Thr Ala Val His Gly Ile Gln Ser Ala Phe Asp Glu Ala Met Ser Tyr  
 115 120 125  
 Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp Trp His Phe Lys Asp His  
 130 135 140  
 Glu Glu Gln Asp Lys Val Arg Pro Lys Ala Lys Arg Lys Glu Glu Pro  
 145 150 155 160  
 Ser Ser Ile Phe Gln Arg Gln Arg Val Asp Ala Leu Leu Leu Asp Leu  
 165 170 175  
 Arg Gln Lys Phe Pro Pro Lys Phe Val Gln Leu Lys Pro Gly Glu Lys  
 180 185 190  
 Pro Val Pro Val Asp Gln Thr Lys Lys Glu Ala Glu Pro Ile Pro Glu  
 195 200 205  
 Thr Val Lys Pro Glu Glu Lys Glu Thr Thr Lys Asn Val Gln Gln Thr  
 210 215 220  
 Val Ser Ala Lys Gly Pro Pro Glu Lys Arg Met Arg Leu Gln  
 225 230 235  
 <210> 38  
 <211> 202  
 <212> PRT  
 <213> Homo sapiens  
 <400> 38  
 Lys Gly Ser Glu Gly Glu Asn Pro Leu Thr Val Pro Gly Arg Glu Lys  
 1 5 10 15  
 Glu Gly Met Leu Met Gly Val Lys Pro Gly Glu Asp Ala Ser Gly Pro  
 20 25 30  
 Ala Glu Asp Leu Val Arg Arg Ser Glu Lys Asp Thr Ala Ala Val Val  
 35 40 45  
 Ser Arg Gln Gly Ser Ser Leu Asn Leu Phe Glu Asp Val Gln Ile Thr  
 50 55 60  
 Glu Pro Glu Ala Glu Pro Glu Ser Lys Ser Glu Pro Arg Pro Pro Ile  
 65 70 75 80

Ser Ser Pro Arg Ala Pro Gln Thr Arg Ala Val Lys Pro Arg Leu His  
 85 90 95  
 Pro Val Lys Pro Met Asn Ala Thr Ala Thr Lys Val Ala Asn Cys Ser  
 100 105 110  
 Leu Gly Thr Ala Thr Ile Ile Gly Glu Asn Leu Asn Asn Glu Val Met  
 115 120 125  
 Met Lys Lys Tyr Ser Pro Ser Asp Pro Ala Phe Ala Tyr Ala Gln Leu  
 130 135 140  
 Thr His Asp Glu Leu Ile Gln Leu Val Leu Lys Gln Lys Glu Thr Ile  
 145 150 155 160  
 Ser Lys Lys Glu Phe Gln Val Arg Glu Leu Glu Asp Tyr Ile Asp Asn  
 165 170 175  
 Leu Leu Val Arg Val Met Glu Glu Thr Pro Asn Ile Leu Arg Ile Pro  
 180 185 190  
 Thr Gln Val Gly Lys Lys Ala Gly Lys Met  
 195 200

<210> 39  
 <211> 243  
 <212> PRT  
 <213> Homo sapiens

<400> 39  
 Val Asn Ala Leu Gly Ile Met Ala Ala Val Asp Ile Arg Asp Asn Leu  
 1 5 10 15  
 Leu Gly Ile Ser Trp Val Asp Ser Ser Trp Ile Pro Ile Leu Asn Ser  
 20 25 30  
 Gly Ser Val Leu Asp Tyr Phe Ser Glu Arg Ser Asn Pro Phe Tyr Asp  
 35 40 45  
 Arg Thr Cys Asn Asn Glu Val Val Lys Met Gln Arg Leu Thr Leu Glu  
 50 55 60  
 His Leu Asn Gln Met Val Gly Ile Glu Tyr Ile Leu Leu His Ala Gln  
 65 70 75 80  
 Glu Pro Ile Leu Phe Ile Ile Arg Lys Gln Gln Arg Gln Ser Pro Ala  
 85 90 95  
 Gln Val Ile Pro Leu Ala Asp Tyr Tyr Ile Ile Ala Gly Val Ile Tyr  
 100 105 110  
 Gln Ala Pro Asp Leu Gly Ser Val Ile Asn Ser Arg Val Leu Thr Ala  
 115 120 125

Val His Gly Ile Gln Ser Ala Phe Asp Glu Ala Met Ser Tyr Cys Arg  
 130 135 140

Tyr His Pro Ser Lys Gly Tyr Trp Trp His Phe Lys Asp His Glu Glu  
 145 150 155 160

Gln Asp Lys Val Arg Pro Lys Ala Lys Arg Lys Glu Glu Pro Ser Ser  
 165 170 175

Ile Phe Gln Arg Gln Arg Val Asp Ala Leu Leu Leu Asp Leu Arg Gln  
 180 185 190

Lys Ile Ser Thr Gln Ile Cys Ala Val Asp Gln Thr Lys Lys Glu Ala  
 195 200 205

Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr Lys  
 210 215 220

Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg Met  
 225 230 235 240

Arg Leu Gln

<210> 40

<211> 245

<212> PRT

<213> Homo sapiens

<400> 40

Ala Ala Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp  
 1 5 10 15

Ser Ser Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe  
 20 25 30

Ser Glu Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val  
 35 40 45

Val Lys Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly  
 50 55 60

Ile Glu Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile  
 65 70 75 80

Arg Lys Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp  
 85 90 95

Tyr Tyr Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser  
 100 105 110

Val Ile Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala  
 115 120 125

Phe Asp Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr  
 130 135 140  
 Trp Trp His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys  
 145 150 155 160  
 Ala Lys Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val  
 165 170 175  
 Asp Ala Leu Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val  
 180 185 190  
 Gln Leu Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys  
 195 200 205  
 Glu Ala Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr  
 210 215 220  
 Thr Lys Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys  
 225 230 235 240  
 Arg Met Arg Leu Gln  
 245  
 <210> 41  
 <211> 163  
 <212> PRT  
 <213> Homo sapiens  
 <400> 41  
 Gly Glu Arg Gln Gly Leu Val Ala Arg Ala Arg Leu Ser Leu Arg Pro  
 1 5 10 15  
 Ser Ile Pro Glu Leu Ser Glu Arg Thr Ser Arg Pro Cys Arg Ala Ser  
 20 25 30  
 Pro Ala Ser Leu Pro Ser Gln His Thr Ser Ser Pro Ala Gln Ala Arg  
 35 40 45  
 Val Arg Asn Leu Ala Gln Ser Thr Phe Pro Leu Ala Ala Gln Glu Thr  
 50 55 60  
 Pro Gly Arg Ala Pro Ala His Ala Pro Leu Ser Ser Phe Val Pro Gly  
 65 70 75 80  
 Val Gly Gly Arg Ser Pro Ala Ser Val Gly Ile Ser Ala Pro Gly Gly  
 85 90 95  
 Gly Pro Ser Gly Ala Ala Ala Lys Ile Pro Leu Glu Leu Thr Gln Ser  
 100 105 110  
 Arg Val Gln Lys Ile Trp Val Pro Val Asp His Arg Pro Ser Leu Pro  
 115 120 125  
 Arg Ser Cys Gly Pro Lys Leu Thr Asn Ser Pro Ala Val Phe Val Met

130

135

140

Val Gly Leu Pro Arg Pro Gly Gln Asp Leu Leu Leu His Glu Ser Leu  
 145 150 155 160

Leu Ala Ala

<210> 42

<211> 243

<212> PRT

<213> Homo sapiens

<400> 42

Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser Ser  
 1 5 10 15

Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser Glu  
 20 25 30

Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val Val Lys  
 35 40 45

Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly Ile Glu  
 50 55 60

Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg Lys  
 65 70 75 80

Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr Tyr  
 85 90 95

Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val Ile  
 100 105 110

Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala Phe Asp  
 115 120 125

Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp Trp  
 130 135 140

His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys Ala Lys  
 145 150 155 160

Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val Asp Ala  
 165 170 175

Leu Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val Gln Leu  
 180 185 190

Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys Glu Ala  
 195 200 205

Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr Lys  
 210 215 220

Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg Met  
 225 230 235 240

Arg Leu Gln

<210> 43  
 <211> 244  
 <212> PRT  
 <213> Homo sapiens

<400> 43

Ala Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser  
 1 5 10 15

Ser Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser  
 20 25 30

Glu Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val Val  
 35 40 45

Lys Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly Ile  
 50 55 60

Glu Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg  
 65 70 75 80

Lys Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr  
 85 90 95

Tyr Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val  
 100 105 110

Ile Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala Phe  
 115 120 125

Asp Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp  
 130 135 140

Trp His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys Ala  
 145 150 155 160

Lys Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val Asp  
 165 170 175

Ala Leu Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val Gln  
 180 185 190

Leu Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys Glu  
 195 200 205

Ala Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr  
 210 215 220

Lys Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg  
 225 230 235 240

Met Arg Leu Gln

<210> 44  
 <211> 109  
 <212> PRT  
 <213> Homo sapiens

<400> 44  
 Glu Leu His Phe Ser Glu Phe Thr Ser Ala Val Ala Asp Met Lys Asn  
 1 5 10 15

Ser Val Ala Asp Arg Asp Asn Ser Pro Ser Ser Cys Ala Gly Leu Phe  
 20 25 30

Ile Ala Ser His Ile Gly Phe Asp Trp Pro Gly Val Trp Val His Leu  
 35 40 45

Asp Ile Ala Ala Pro Val His Ala Gly Glu Arg Ala Thr Gly Phe Gly  
 50 55 60

Val Ala Leu Leu Leu Ala Leu Phe Gly Arg Ala Ser Glu Asp Pro Leu  
 65 70 75 80

Leu Asn Leu Val Ser Pro Leu Asp Cys Glu Val Asp Ala Gln Glu Gly  
 85 90 95

Asp Asn Met Gly Arg Asp Ser Lys Arg Arg Arg Leu Val  
 100 105

<210> 45  
 <211> 324  
 <212> PRT  
 <213> Homo sapiens

<400> 45  
 Arg Arg Pro Val Met Ala Gln Glu Thr Ala Pro Pro Cys Gly Pro Val  
 1 5 10 15

Ser Arg Gly Asp Ser Pro Ile Ile Glu Lys Met Glu Lys Arg Thr Cys  
 20 25 30

Ala Leu Cys Pro Glu Gly His Glu Trp Ser Gln Ile Tyr Phe Ser Pro  
 35 40 45

Ser Gly Asn Ile Val Ala His Glu Asn Cys Leu Leu Tyr Ser Ser Gly  
 50 55 60

Leu Val Glu Cys Glu Thr Leu Asp Leu Arg Asn Thr Ile Arg Asn Phe  
 65 70 75 80



Asp Val Lys Ser Val Lys Lys Glu Ile Trp Arg Gly Arg Arg Leu Lys  
                             85                            90                            95  
 Cys Ser Phe Cys Asn Lys Gly Gly Ala Thr Val Gly Cys Asp Leu Trp  
                             100                            105                            110  
 Phe Cys Lys Lys Ser Tyr His Tyr Val Cys Ala Lys Lys Asp Gln Ala  
                             115                            120                            125  
 Ile Leu Gln Val Asp Gly Asn His Gly Thr Tyr Lys Leu Phe Cys Pro  
                             130                            135                            140  
 Glu His Ser Pro Glu Gln Glu Glu Ala Thr Glu Ser Ala Asp Asp Pro  
                             145                            150                            155                            160  
 Ser Met Lys Lys Lys Arg Gly Lys Asn Lys Arg Leu Ser Ser Gly Pro  
                             165                            170                            175  
 Pro Ala Gln Pro Lys Thr Met Lys Cys Ser Asn Ala Lys Arg His Met  
                             180                            185                            190  
 Thr Glu Glu Pro His Gly His Thr Asp Ala Ala Val Lys Ser Pro Phe  
                             195                            200                            205  
 Leu Lys Lys Cys Gln Glu Ala Gly Leu Leu Thr Glu Leu Phe Glu His  
                             210                            215                            220  
 Ile Leu Glu Asn Met Asp Ser Val His Gly Arg Leu Val Asp Glu Thr  
                             225                            230                            235                            240  
 Ala Ser Glu Ser Asp Tyr Glu Gly Ile Glu Thr Leu Leu Phe Asp Cys  
                             245                            250                            255  
 Gly Leu Phe Lys Asp Thr Leu Arg Lys Phe Gln Glu Val Ile Lys Ser  
                             260                            265                            270  
 Lys Ala Cys Glu Trp Glu Glu Arg Gln Arg Gln Met Lys Gln Gln Leu  
                             275                            280                            285  
 Glu Ala Leu Ala Asp Leu Gln Gln Ser Leu Cys Ser Phe Gln Glu Asn  
                             290                            295                            300  
 Gly Asp Leu Asp Cys Ser Ser Ser Thr Ser Gly Ser Leu Leu Pro Pro  
                             305                            310                            315                            320  
 Glu Asp His Gln

&lt;210&gt; 46

&lt;211&gt; 244

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 46

Ala Val Asp Ile Arg Asp Asn Leu Leu Gly Ile Ser Trp Val Asp Ser

25

1                      5                      10                      15  
 Ser Trp Ile Pro Ile Leu Asn Ser Gly Ser Val Leu Asp Tyr Phe Ser  
                          20                      25                      30  
 Glu Arg Ser Asn Pro Phe Tyr Asp Arg Thr Cys Asn Asn Glu Val Val  
                          35                      40                      45  
 Lys Met Gln Arg Leu Thr Leu Glu His Leu Asn Gln Met Val Gly Ile  
                          50                      55                      60  
 Glu Tyr Ile Leu Leu His Ala Gln Glu Pro Ile Leu Phe Ile Ile Arg  
                          65                      70                      75                      80  
 Lys Gln Gln Arg Gln Ser Pro Ala Gln Val Ile Pro Leu Ala Asp Tyr  
    85                      90                      95  
 Tyr Ile Ile Ala Gly Val Ile Tyr Gln Ala Pro Asp Leu Gly Ser Val  
    100                      105                      110  
 Ile Asn Ser Arg Val Leu Thr Ala Val His Gly Ile Gln Ser Ala Phe  
    115                      120                      125  
 Asp Glu Ala Met Ser Tyr Cys Arg Tyr His Pro Ser Lys Gly Tyr Trp  
    130                      135                      140  
 Trp His Phe Lys Asp His Glu Glu Gln Asp Lys Val Arg Pro Lys Ala  
    145                      150                      155                      160  
 Lys Arg Lys Glu Glu Pro Ser Ser Ile Phe Gln Arg Gln Arg Val Asp  
    165                      170                      175  
 Ala Leu Leu Leu Asp Leu Arg Gln Lys Phe Pro Pro Lys Phe Val Gln  
    180                      185                      190  
 Leu Lys Pro Gly Glu Lys Pro Val Pro Val Asp Gln Thr Lys Lys Glu  
    195                      200                      205  
 Ala Glu Pro Ile Pro Glu Thr Val Lys Pro Glu Glu Lys Glu Thr Thr  
    210                      215                      220  
 Lys Asn Val Gln Gln Thr Val Ser Ala Lys Gly Pro Pro Glu Lys Arg  
    225                      230                      235                      240  
 Met Arg Leu Gln

&lt;210&gt; 47

&lt;211&gt; 14

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

tttttttttt ttag

14

<210> 48  
<211> 10  
<212> DNA  
<213> Homo sapiens

<400> 48  
cttcaacctc

10

<210> 49  
<211> 496  
<212> DNA  
<213> Homo sapiens

<400> 49  
gcaccatgta ccgagcactt cggctcctcg cgcgctcgcg tccccctcgtg cgggctccag 60  
ccgcagcctt agcttcgggt cccggcttgg gtggcgcggt cgtgccctcg ttttggcctc 120  
cgaacgcggc tcgaatggca agccaaaatt ccttcgggat agaatatgat acctttgggt 180  
aactaaaggt gccaaatgat aagtattatg gcgcccagac cgtgagatct acgatgaact 240  
ttaagattgg aggtgtgaca gaacgcctgc caacccagcgt tattaaagct tttggcatct 300  
tgaagcgagc ggccgctgaa gttaaccagg attatggctc tgatccaaag attgctaatt 360  
caataatgaa ggcagcagat gaggtagctg aaggtaaatt aaatgatcat tttcctctcg 420  
tggtatggca gactggatca ggaactcaga caaatatgaa tgtaaatgaa gtcattagcc 480  
aatagagcaa ttgaaa 496

<210> 50  
<211> 499  
<212> DNA  
<213> Homo sapiens

<400> 50  
agaaaaagtc tatgtttgca gaaatacaga tccaagacaa agacaggatg ggcactgctg 60  
gaaaagttat taaatgcaaa gcagctgtgc tttgggagca gaagcaaccc ttctccattg 120  
aggaaataga agttgcccc ccaaagacta aagaagttcg cattaagatt ttggccacag 180  
gaatctgtcg cacagatgac catgtgataa aaggaacaat ggtgtccaag tttccagtga 240  
ttgtgggaca tgaggcaact gggattgtag agagcattgg agaaggagt actacagtga 300  
aaccagggtg caaagtcate cctctcttc tgccacaatg tagagaatgc aatgcttgc 360  
gcaaccaga tggcaacctt tgcattagga gcgatattac tggctcgtga gtactggctg 420  
atggcaccac cagatttaca tgcaagggcg aaccagtcca ccacttcag aacaccagta 480  
catttaccga gtacacagt 499

<210> 51  
<211> 887  
<212> DNA  
<213> Homo sapiens

<400> 51  
gagctctgagc agaaaggaaa agcagccttg gcagccacgt tagaggaata caaagccaca 60  
gtggccagt accagataga gatgaatcgc ctgaaggctc agctggagaa tgaaaagcag 120  
aaagtggcag agctgtattc tatccataac tctggagaca aatctgatat tcaggacctc 180  
ctggagagtg tcaggctgga caaagaaaaa gcagagactt tggctagtag cttgcaggaa 240  
gatctggctc ataccgaaa tgatgccaat cgattacagg atgccattgc taaggtagag 300  
gatgaatacc gagccttcca agaagaagct aagaaacaaa ttgaagattt gaatatgacg 360  
ttagaaaaat taagatcaga cctggatgaa aaagaaacag aaaggagtga catgaaagaa 420  
accatctttg aacttgaaga tgaagtagaa caacatcgtg ctgtgaaact tcatgacaac 480  
ctcattattt ctgatctaga gaatacagtt aaaaaactcc aggacaaaa gcacgacatg 540

gaaagagaaa taaagacact ccacagaaga cttcgggaag aatctgcgga atggcggcag 600  
tttcaggctg atctccagac tgcagtagtc attgcaaatg acattaaatc tgaagcccaa 660  
gaggagattg gtgatctaaa gcgccgggta catgaggctc aagaaaaaaa tgagaaactc 720  
acaaaagaat tggaggaaat aaagtcacgc aagcaagagg aggagcgagg cggtatata 780  
attacatgaa tgccgttgag agagatttgg cagccttaag gcaggggaatg ggactgagta 840  
gaaggtcctc gacttcctca gagccaactc ctacagtaaa aaccctc 887

<210> 52  
<211> 491  
<212> DNA  
<213> Homo sapiens

<400> 52  
ggcacgagct ttccaaaaa tcatgctgct cttttctcta aagttcttac attttataga 60  
aaggaaacct tcactcttga ggcctactac agctctctc aggatttggc ctatccagat 120  
cctgctatag ctcagttttc agttcagaaa gtcactccbc agtctgatgg ctccagtcca 180  
aaagtgaag tcaaagtctg agtaaatgtc catggcattt tcagtgtgtc cagtgcattc 240  
ttagtggagg ttcacaagtc tgaggaaaat gaggagccaa tggaaacaga tcagaatgca 300  
aaggaggaag agaagatgca agtggaccag gaggaaccac atgttgaaga gcaacagcag 360  
cagacaccag gcagaaaata aggcagagtc tgaagaaatg gagaacctc aagctggatc 420  
caaggataaa aagatggacc aaccacccca agccaagaag gcaaaagtga agaccagtae 480  
tgtggacctg g 491

<210> 53  
<211> 787  
<212> DNA  
<213> Homo sapiens

<400> 53  
aagcagttga gtaggcagaa aaaagaacct cttcattaag gattaaaatg tataggccag 60  
cacgtgtaac ttcgacttca agattttctga atccatatgt agtatgtttc attgtcgtcg 120  
caggggtagt gatcctggca gtcaccatag ctctacttgt ttacttttta gcttttgatc 180  
aaaaatctta cttttatagg agcagttttc aactcctaaa tgttgaatat aatagtcagt 240  
taaattcacc agctacacag gaatacagga ctttgagtgg aagaattgaa tctctgatta 300  
ctaaaacatt caaagaatca aatttaagaa atcagttcat cagagctcat gttgccaaac 360  
tgaggcaaga tggtagtggg gtgagagcgg atgttgtcat gaaatttcaa ttcactagaa 420  
ataacaatgg agcatcaatg aaaagcagaa ttgagtctgt ttacgacaa atgctgaata 480  
actctggaaa cctggaaata aacccttcaa ctgagataac atcacttact gaccaggctg 540  
cagcaaatgg gcttattaat gaatgtgggg ccggtccaga cctaataaca ttgtctgagc 600  
agagaatcct tggaggcact gaggtcgagg agggagctg gccgtggcaa gtcagctctg 660  
ggctcaataa tgcccaccac tgtggaggca gcctgatcaa taacatgtgg atcctgacag 720  
cagctcactg cttcagaagc aactctaate ctcgtgactg gattgccacg tctggtattt 780  
ccacaac 787

<210> 54  
<211> 386  
<212> DNA  
<213> Homo sapiens

<400> 54  
ggcattttca gtgtgtccag tgcattctta gtggaggttc acaagtctga ggaaaatgag 60  
gagccaatgg aaacagatca gaatgcaaag gaggaagaga agatgcaagt ggaccaggag 120  
gaaccacatg ttgaagagca acagcagcag acaccagcag aaaataaggc agagcttgaa 180  
gaaatggaga cctctcaagc tggatccaag gataaaaaga tggaccaacc accccaagcc 240  
aagaaggcaa aagtgaagac cagtactgtg gacctgcaa tcgagaatca gctattatgg 300

cagatagaca gagagatgct caacttgtagc attgaaaatg agggtaagat gatcatgcag 360  
gataaactgg agaaggagcg gaatga 386

<210> 55

<211> 1462

<212> DNA

<213> Homo sapiens

<400> 55

aagcagttga gtaggcagaa aaaagaacct cttcattaag gattaaaatg tataggccag 60  
cacgtgtaac ttcgacttca agatttctga atccatatgt agtatgtttc attgtcgtcg 120  
caggggtagt gatcctggca gtcaccatag ctctacttgt ttacttttta gcttttgatc 180  
aaaaatctta cttttatagg agcagttttc aactcctaaa tgttgaatat aatagtcagt 240  
taaattcacc agctacacag gaatacagga ctttgagtgg aagaattgaa tctctgatta 300  
ctaaaacatt caaagaatca aatttaagaa atcagttcat cagagctcat gttgccaaac 360  
tgaggcaaga tggtagtggg gtgagagcgg atgttgctcat gaaatttcaa ttcactagaa 420  
ataacaatgg agcatcaatg aaaagcagaa ttgagtctgt ttacgacaa atgctgaata 480  
actctggaaa cctggaaata aacccttcaa ctgagataac atcacttact gaccaggctg 540  
cagcaaatgg gcttattaat gaatgtgggg ccggtccaga cctaataaca ttgtctgagc 600  
agagaatcct tggaggcact gaggctgagg agggaaagctg gccgtggcaa gtcagtctgc 660  
ggctcaataa tgcccaccac tgtggaggca gcctgatcaa taacatgtgg atcctgacag 720  
cagctcactg cttcagaagc aactctaate ctctgtactg gattgccacg tctgggtattt 780  
ccacaacatt tcctaaacta agaatagagag taagaaatat tttaattcat aacaattata 840  
aatctgcaac tcatgaaaat gacattgcac ttgtgagact tgagaacagt gtcaccttta 900  
ccaaagatat ccatagtgtg tgtctcccag ctgctaccca gaataattcca cctgggtcta 960  
ctgcttatgt aacaggatgg ggcgctcaag aatatgctgg ccacacagtt ccagagctaa 1020  
ggcaaggaca ggtcagaata ataagtaatg atgatatgaa tgcaccacat agttataatg 1080  
gagccatctt gtctggaatg ctgtgtgctg gagtacctca aggtggagtg gacgcatgtc 1140  
agggtgactc tgggtggcca ctagtacaag aagactcacg gcggctttgg ttattgtgg 1200  
ggatagtaag ctggggagat cagtgtggcc tgccggataa gccaggagtg tatactcgag 1260  
tgacagcata cattgactgg attaggcaac aaactgggat ctagtgcaac aagtgcattc 1320  
ctgttgcaaa gtctgtatgc aggtgtgcct gtcttaaat ccaaagcttt acatttcaac 1380  
tgaaaaagaa actagaaatg tcctaattta acatcttgtt acataaatat ggtttaacaa 1440  
aaaaaaaaa aaaaaactcg ag 1462

<210> 56

<211> 159

<212> PRT

<213> Homo sapiens

<400> 56

Thr Met Tyr Arg Ala Leu Arg Leu Leu Ala Arg Ser Arg Pro Leu Val  
1 5 10 15

Arg Ala Pro Ala Ala Ala Leu Ala Ser Ala Pro Gly Leu Gly Gly Ala  
20 25 30

Ala Val Pro Ser Phe Trp Pro Pro Asn Ala Ala Arg Met Ala Ser Gln  
35 40 45

Asn Ser Phe Arg Ile Glu Tyr Asp Thr Phe Gly Glu Leu Lys Val Pro  
50 55 60

Asn Asp Lys Tyr Tyr Gly Ala Gln Thr Val Arg Ser Thr Met Asn Phe  
65 70 75 80

Lys Ile Gly Gly Val Thr Glu Arg Met Pro Thr Pro Val Ile Lys Ala  
85 90 95

Phe Gly Ile Leu Lys Arg Ala Ala Ala Glu Val Asn Gln Asp Tyr Gly  
100 105 110

Leu Asp Pro Lys Ile Ala Asn Ala Ile Met Lys Ala Ala Asp Glu Val  
115 120 125

Ala Glu Gly Lys Leu Asn Asp His Phe Pro Leu Val Val Trp Gln Thr  
130 135 140

Gly Ser Gly Thr Gln Thr Asn Met Asn Val Asn Glu Val Ile Ser  
145 150 155

<210> 57

<211> 165

<212> PRT

<213> Homo sapiens

<400> 57

Lys Lys Ser Met Phe Ala Glu Ile Gln Ile Gln Asp Lys Asp Arg Met  
1 5 10 15

Gly Thr Ala Gly Lys Val Ile Lys Cys Lys Ala Ala Val Leu Trp Glu  
20 25 30

Gln Lys Gln Pro Phe Ser Ile Glu Glu Ile Glu Val Ala Pro Pro Lys  
35 40 45

Thr Lys Glu Val Arg Ile Lys Ile Leu Ala Thr Gly Ile Cys Arg Thr  
50 55 60

Asp Asp His Val Ile Lys Gly Thr Met Val Ser Lys Phe Pro Val Ile  
65 70 75 80

Val Gly His Glu Ala Thr Gly Ile Val Glu Ser Ile Gly Glu Gly Val  
85 90 95

Thr Thr Val Lys Pro Gly Asp Lys Val Ile Pro Leu Phe Leu Pro Gln  
100 105 110

Cys Arg Glu Cys Asn Ala Cys Arg Asn Pro Asp Gly Asn Leu Cys Ile  
115 120 125

Arg Ser Asp Ile Thr Gly Arg Gly Val Leu Ala Asp Gly Thr Thr Arg  
130 135 140

Phe Thr Cys Lys Gly Glu Pro Val His His Phe Met Asn Thr Ser Thr  
145 150 155 160

Phe Thr Glu Tyr Thr  
165

<210> 58  
 <211> 259  
 <212> PRT  
 <213> Homo sapiens

<400> 58

Glu Ser Glu Gln Lys Gly Lys Ala Ala Leu Ala Ala Thr Leu Glu Glu  
 1 5 10 15

Tyr Lys Ala Thr Val Ala Ser Asp Gln Ile Glu Met Asn Arg Leu Lys  
 20 25 30

Ala Gln Leu Glu Asn Glu Lys Gln Lys Val Ala Glu Leu Tyr Ser Ile  
 35 40 45

His Asn Ser Gly Asp Lys Ser Asp Ile Gln Asp Leu Leu Glu Ser Val  
 50 55 60

Arg Leu Asp Lys Glu Lys Ala Glu Thr Leu Ala Ser Ser Leu Gln Glu  
 65 70 75 80

Asp Leu Ala His Thr Arg Asn Asp Ala Asn Arg Leu Gln Asp Ala Ile  
 85 90 95

Ala Lys Val Glu Asp Glu Tyr Arg Ala Phe Gln Glu Glu Ala Lys Lys  
 100 105 110

Gln Ile Glu Asp Leu Asn Met Thr Leu Glu Lys Leu Arg Ser Asp Leu  
 115 120 125

Asp Glu Lys Glu Thr Glu Arg Ser Asp Met Lys Glu Thr Ile Phe Glu  
 130 135 140

Leu Glu Asp Glu Val Glu Gln His Arg Ala Val Lys Leu His Asp Asn  
 145 150 155 160

Leu Ile Ile Ser Asp Leu Glu Asn Thr Val Lys Lys Leu Gln Asp Gln  
 165 170 175

Lys His Asp Met Glu Arg Glu Ile Lys Thr Leu His Arg Arg Leu Arg  
 180 185 190

Glu Glu Ser Ala Glu Trp Arg Gln Phe Gln Ala Asp Leu Gln Thr Ala  
 195 200 205

Val Val Ile Ala Asn Asp Ile Lys Ser Glu Ala Gln Glu Glu Ile Gly  
 210 215 220

Asp Leu Lys Arg Arg Leu His Glu Ala Gln Glu Lys Asn Glu Lys Leu  
 225 230 235 240

Thr Lys Glu Leu Glu Glu Ile Lys Ser Arg Lys Gln Glu Glu Glu Arg  
 245 250 255

Gly Gly Tyr

<210> 59  
 <211> 125  
 <212> PRT  
 <213> Homo sapiens

<400> 59

Gly	Thr	Ser	Phe	Ser	Lys	Asn	His	Ala	Ala	Pro	Phe	Ser	Lys	Val	Leu
1				5					10					15	
Thr	Phe	Tyr	Arg	Lys	Glu	Pro	Phe	Thr	Leu	Glu	Ala	Tyr	Tyr	Ser	Ser
			20					25					30		
Pro	Gln	Asp	Leu	Pro	Tyr	Pro	Asp	Pro	Ala	Ile	Ala	Gln	Phe	Ser	Val
	35					40	--					45			
Gln	Lys	Val	Thr	Pro	Gln	Ser	Asp	Gly	Ser	Ser	Ser	Lys	Val	Lys	Val
	50					55					60				
Lys	Val	Arg	Val	Asn	Val	His	Gly	Ile	Phe	Ser	Val	Ser	Ser	Ala	Ser
65				70					75					80	
Leu	Val	Glu	Val	His	Lys	Ser	Glu	Glu	Asn	Glu	Glu	Pro	Met	Glu	Thr
			85					90						95	
Asp	Gln	Asn	Ala	Lys	Glu	Glu	Glu	Lys	Met	Gln	Val	Asp	Gln	Glu	Glu
		100					105					110			
Pro	His	Val	Glu	Glu	Gln	Gln	Gln	Gln	Thr	Pro	Gly	Arg			
	115					120					125				

<210> 60  
 <211> 246  
 <212> PRT  
 <213> Homo sapiens

<400> 60

Met	Tyr	Arg	Pro	Ala	Arg	Val	Thr	Ser	Thr	Ser	Arg	Phe	Leu	Asn	Pro
1				5					10					15	
Tyr	Val	Val	Cys	Phe	Ile	Val	Val	Ala	Gly	Val	Val	Ile	Leu	Ala	Val
			20					25					30		
Thr	Ile	Ala	Leu	Leu	Val	Tyr	Phe	Leu	Ala	Phe	Asp	Gln	Lys	Ser	Tyr
	35					40						45			
Phe	Tyr	Arg	Ser	Ser	Phe	Gln	Leu	Leu	Asn	Val	Glu	Tyr	Asn	Ser	Gln
	50					55					60				
Leu	Asn	Ser	Pro	Ala	Thr	Gln	Glu	Tyr	Arg	Thr	Leu	Ser	Gly	Arg	Ile
65				70					75					80	



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<210> 61
<211> 128
<212> PRT
<213> Homo sapiens
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<400> 61

Gly Ile Phe Ser Val Ser Ser Ala Ser Leu Val Glu Val His Lys Ser  
1 5 10 15

Glu Glu Asn Glu Glu Pro Met Glu Thr Asp Gln Asn Ala Lys Glu Glu  
20 25 30

Glu Lys Met Gln Val Asp Gln Glu Glu Pro His Val Glu Glu Gln Gln  
35 40 45

Gln Gln Thr Pro Ala Glu Asn Lys Ala Glu Ser Glu Glu Met Glu Thr  
50 55 60

Ser Gln Ala Gly Ser Lys Asp Lys Lys Met Asp Gln Pro Pro Gln Ala  
65 70 75 80

Lys Lys Ala Lys Val Lys Thr Ser Thr Val Asp Leu Pro Ile Glu Asn

85 90 95  
 Gln Leu Leu Trp Gln Ile Asp Arg Glu Met Leu Asn Leu Tyr Ile Glu  
 100 105 110  
 Asn Glu Gly Lys Met Ile Met Gln Asp Lys Leu Glu Lys Glu Arg Asn  
 115 120 125  
  
 <210> 62  
 <211> 418  
 <212> PRT  
 <213> Homo sapiens  
  
 <400> 62  
 Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro  
 1 5 10 15  
 Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val  
 20 25 30  
 Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr  
 35 40 45  
 Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln  
 50 55 60  
 Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile  
 65 70 75 80  
 Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln  
 85 90 95  
 Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val  
 100 105 110  
 Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly  
 115 120 125  
 Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn  
 130 135 140  
 Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu  
 145 150 155 160  
 Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly  
 165 170 175  
 Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu  
 180 185 190  
 Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn  
 195 200 205  
 Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr

210                      215                      220  
 Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala  
 225                      230                      235                      240  
 Thr Ser Gly Ile Ser Thr Thr Phe Pro Lys Leu Arg Met Arg Val Arg  
                     245                      250                      255  
 Asn Ile Leu Ile His Asn Asn Tyr Lys Ser Ala Thr His Glu Asn Asp  
                     260                      265                      270  
 Ile Ala Leu Val Arg Leu Glu Asn Ser Val Thr Phe Thr Lys Asp Ile  
                     275                      280                      285  
 His Ser Val Cys Leu Pro Ala Ala Thr Gln Asn Ile Pro Pro Gly Ser  
                     290                      295                      300  
 Thr Ala Tyr Val Thr Gly Trp Gly Ala Gln Glu Tyr Ala Gly His Thr  
 305                      310                      315                      320  
 Val Pro Glu Leu Arg Gln Gly Gln Val Arg Ile Ile Ser Asn Asp Val  
                     325                      330                      335  
 Cys Asn Ala Pro His Ser Tyr Asn Gly Ala Ile Leu Ser Gly Met Leu  
                     340                      345                      350  
 Cys Ala Gly Val Pro Gln Gly Gly Val Asp Ala Cys Gln Gly Asp Ser  
                     355                      360                      365  
 Gly Gly Pro Leu Val Gln Glu Asp Ser Arg Arg Leu Trp Phe Ile Val  
                     370                      375                      380  
 Gly Ile Val Ser Trp Gly Asp Gln Cys Gly Leu Pro Asp Lys Pro Gly  
 385                      390                      395                      400  
 Val Tyr Thr Arg Val Thr Ala Tyr Ile Asp Trp Ile Arg Gln Gln Thr  
                     405                      410                      415

Gly Ile

<210> 63

<211> 776

<212> DNA

<213> Homo sapiens

<400> 63

cacagatggt gatagaggaa tccatcttgc agtcagataa agccctcact gatagagaga 60  
 aggcagtagc agtggatcgg gccaagaagg aggcagctga gaaggaacag gaacttttaa 120  
 aacagaaatt acaggagcag ccagcaacag atggaggctc aagataagag tcgcaaggaa 180  
 aactagccaa ctgaaggaga agctgcagat ggagagagaa cacctactga gagagcagat 240  
 tatgatgttg gagcacacgc agaaggtcca aaatgatttg cttcatgaag gatttaagaa 300  
 gaagtatgag gagatgaatg cagagataag tcaatttaaa cgtatgattg atactacaaa 360  
 aaatgatgat actcctgga ttgcacgaac cttggacaac cttgccgatg agctaactgc 420  
 aatattgtct gctcctgcta aattaattgg tcatggtgtc aaaggtgtga gctcactctt 480

taaaaagcat aagctcccct ttttaaggata ttatagattg tacatatatg ctttggacta 540  
 tttttgatct gtatgttttt cattttcatt cagcaagttt tttttttttt tcagagtctt 600  
 actctgttgc ccaggctgga gtacagtggg gcaatctcag ctactgcaa cctctgcctc 660  
 ctgggttcaa gagattcacc tgctcagcc ccctagtagc tgggattata ggtgtacacc 720  
 accacacca gctaattttt gtatttttag tagagatggg gtttcactat gttggc 776

&lt;210&gt; 64

&lt;211&gt; 160

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 64

gcagcgctct cggttgcagt acccactgga aggacttagg cgctcgctg gacaccgcaa 60  
 gccctcagt agcctcggcc caagaggcct gctttccact cgctagcccc gccgggggtc 120  
 cgtgtcctgt ctcggtgccc ggaccgggc ccgagcaga 160

&lt;210&gt; 65

&lt;211&gt; 72

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 65

Leu Ser Ala Met Gly Phe Thr Ala Ala Gly Ile Ala Ser Ser Ser Ile  
 1 5 10 15

Ala Ala Lys Met Met Ser Ala Ala Ala Ile Ala Asn Gly Gly Gly Val  
 20 25 30

Ala Ser Gly Ser Leu Val Ala Thr Leu Gln Ser Leu Gly Ala Thr Gly  
 35 40 45

Leu Ser Gly Leu Thr Lys Phe Ile Leu Gly Ser Ile Gly Ser Ala Ile  
 50 55 60

Ala Ala Val Ile Ala Arg Phe Tyr  
 65 70

&lt;210&gt; 66

&lt;211&gt; 2581

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 66

ctttcaaccc gcgctcgccg gctccagccc cgcgcgcccc cacccttgc cctcccggcg 60  
 gctccgcagg gtgaggtggc tttgaccccg ggttgcccgg ccagcacgac cgaggaggtg 120  
 gctggacagc tggaggatga acggagaagc cgactgcccc acagacctgg aaatggccgc 180  
 ccccaaagc caagaccgtt ggtcccagga agacatgctg actttgctgg aatgcatgaa 240  
 gaacaacctt ccatccaatg acagctccaa gttcaaaacc accgaatcac acatggactg 300  
 ggaaaaagta gcatttaaag acttttctgg agacatgtgc aagctcaaat ggggtggagat 360  
 ttctaagtag gtgaggaagt tccgtacatt gacagaattg atcctcgatg ctccaggaaca 420  
 tgtaaaaaat ccttacaag gcaaaaaact caagaaacac ccagacttcc caaagaagcc 480  
 cctgaccctt tatttccgct tcttcatgga gaagcggggc aagtatgca aactccacc 540  
 tgagatgagc aacctggacc taaccaagat tctgtccaag aaatacaagg agcttcgga 600  
 gaagaagaag atgaaatata ttcaggactt ccagagagag aaacaggagt tcgagcgaaa 660

cctggcccga ttcaggagg atcaccccga cctaattccag aatgccaaaga aatcggacat 720  
 cccagagaag cccaaaaccc cccagcagct gtggtacacc cacgagaaga aggtgtatct 780  
 caaagtgcgg ccagatgcca ctacgaagga ggtgaaggac tccctgggga agcagtggc 840  
 tcagctctcg gacaaaaaga ggctgaaatg gattcataag gccctggagc agcggaaagga 900  
 gtacgaggag atcatgagag actatatcca gaagcaccca gagctgaaca tcagtgagga 960  
 gggatatcacc aagtccaccc tcaccaaggc cgaacgccag ctcaaggaca agtttgacgg 1020  
 gcgacccacc aagccacctc cgaacagcta ctcgctgtac tgcgcagagc tcatggccaa 1080  
 catgaaggac gtgccagca cagagcgcat ggtgctgtgc agccagcagt ggaagctgct 1140  
 gtcccagaag gagaaggacg cctatcaca gaagtgtgat cagaaaaaga aagattacga 1200  
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 agcccaggaa gggggcaagg gcggtccga gaagcccaag cggcccggtg cggccatgtt 1380  
 catcttctcg gaggagaaac ggcggcagct gcaggaggag cggcctgagc tctccgagag 1440  
 cgagctgacc cgcctgctgg ccggaatgtg gaacgacctg tctgagaaga agaaggccaa 1500  
 gtacaaggcc cgagaggcgg cgctcaaggc tcagtcggag aggaagcccc gcggggagcg 1560  
 cgaggaacgg ggcaagctgc ccgagtcgcc caaaagagct gaggagatct ggcaacagag 1620  
 cgttatcggc gactacctgg ccgcttcaa gaatgacctg gtgaaggcct tgaaagccat 1680  
 ggaaatgacc tggaaataaca tggaaaagaa ggagaaactg atgtggatta agaaggcagc 1740  
 cgaagaccaa aagcgatatg agagagagct gagtgatag cgggcacctc cagctgctac 1800  
 aaattcttcc aagaagatga aattccaggg agaacccea aagcctccca tgaacggtta 1860  
 ccagaagttc tcccaggagc tgctgtccaa tggggagctg aaccacctgc cgctgaagga 1920  
 gcgcattgtg gagatcggca gtcgctggca gcgcattctc cagagccaga aggagcacta 1980  
 caaaaagctg gccgaggagc agcaaaagca gtacaaggtg cacctggacc tctgggttaa 2040  
 gagcctgtct cccaggagcc gtgcagcata taaagagtac atctccaata aacgtaagag 2100  
 catgaccaag ctgcgaggcc caaaccceaa atccagccgg actactctgc agtccaagtc 2160  
 ggagtcaggag gaggatgatg aagaggatga ggatgacgag gacgaggatg aagaagagga 2220  
 agatgatgag aatggggact cctctgaaga tggcgggcag tcctctgagt ccagcagcga 2280  
 ggacgagagc gaggatgggg atgagaatga agaggatgac gaggacgaag acgacgacga 2340  
 ggatgacgat gaggatgaag ataatgagtc cgagggcagc agctccagct cctcctcctt 2400  
 aggggactcc tcagactttg actccaactg aggccttagcc ccacccagc ggagccaggg 2460  
 agagcccagg agctcccctc cccaactgac cacctttgtt tcttccccat gttctgtccc 2520  
 ttgccccctt ggcctcccc actttcttcc tttctttaa aaaaaaaa aaaaactcga 2580  
 g 2581

<210> 67  
 <211> 764  
 <212> PRT  
 <213> Homo sapiens

<400> 67  
 Met Asn Gly Glu Ala Asp Cys Pro Thr Asp Leu Glu Met Ala Ala Pro  
 1 5 10 15  
 Lys Gly Gln Asp Arg Trp Ser Gln Glu Asp Met Leu Thr Leu Leu Glu  
 20 25 30  
 Cys Met Lys Asn Asn Leu Pro Ser Asn Asp Ser Ser Lys Phe Lys Thr  
 35 40 45  
 Thr Glu Ser His Met Asp Trp Glu Lys Val Ala Phe Lys Asp Phe Ser  
 50 55 60  
 Gly Asp Met Cys Lys Leu Lys Trp Val Glu Ile Ser Asn Glu Val Arg  
 65 70 75 80

Lys Phe Arg Thr Leu Thr Glu Leu Ile Leu Asp Ala Gln Glu His Val  
 85 90 95  
 Lys Asn Pro Tyr Lys Gly Lys Lys Leu Lys Lys His Pro Asp Phe Pro  
 100 105 110  
 Lys Lys Pro Leu Thr Pro Tyr Phe Arg Phe Phe Met Glu Lys Arg Ala  
 115 120 125  
 Lys Tyr Ala Lys Leu His Pro Glu Met Ser Asn Leu Asp Leu Thr Lys  
 130 135 140  
 Ile Leu Ser Lys Lys Tyr Lys Glu Leu Pro Glu Lys Lys Lys Met Lys  
 145 150 155 160  
 Tyr Ile Gln Asp Phe Gln Arg Glu Lys Gln Glu Phe Glu Arg Asn Leu  
 165 170 175  
 Ala Arg Phe Arg Glu Asp His Pro Asp Leu Ile Gln Asn Ala Lys Lys  
 180 185 190  
 Ser Asp Ile Pro Glu Lys Pro Lys Thr Pro Gln Gln Leu Trp Tyr Thr  
 195 200 205  
 His Glu Lys Lys Val Tyr Leu Lys Val Arg Pro Asp Ala Thr Thr Lys  
 210 215 220  
 Glu Val Lys Asp Ser Leu Gly Lys Gln Trp Ser Gln Leu Ser Asp Lys  
 225 230 235 240  
 Lys Arg Leu Lys Trp Ile His Lys Ala Leu Glu Gln Arg Lys Glu Tyr  
 245 250 255  
 Glu Glu Ile Met Arg Asp Tyr Ile Gln Lys His Pro Glu Leu Asn Ile  
 260 265 270  
 Ser Glu Glu Gly Ile Thr Lys Ser Thr Leu Thr Lys Ala Glu Arg Gln  
 275 280 285  
 Leu Lys Asp Lys Phe Asp Gly Arg Pro Thr Lys Pro Pro Pro Asn Ser  
 290 295 300  
 Tyr Ser Leu Tyr Cys Ala Glu Leu Met Ala Asn Met Lys Asp Val Pro  
 305 310 315 320  
 Ser Thr Glu Arg Met Val Leu Cys Ser Gln Gln Trp Lys Leu Leu Ser  
 325 330 335  
 Gln Lys Glu Lys Asp Ala Tyr His Lys Lys Cys Asp Gln Lys Lys Lys  
 340 345 350  
 Asp Tyr Glu Val Glu Leu Leu Arg Phe Leu Glu Ser Leu Pro Glu Glu  
 355 360 365  
 Glu Gln Gln Arg Val Leu Gly Glu Glu Lys Met Leu Asn Ile Asn Lys

370                      375                      380  
 Lys Gln Ala Thr Ser Pro Ala Ser Lys Lys Pro Ala Gln Glu Gly Gly  
 385                      390                      395                      400  
 Lys Gly Gly Ser Glu Lys Pro Lys Arg Pro Val Ser Ala Met Phe Ile  
                     405                      410                      415  
 Phe Ser Glu Glu Lys Arg Arg Gln Leu Gln Glu Glu Arg Pro Glu Leu  
                     420                      425                      430  
 Ser Glu Ser Glu Leu Thr Arg Leu Leu Ala Arg Met Trp Asn Asp Leu  
                     435                      440                      445  
 Ser Glu Lys Lys Lys Ala Lys Tyr Lys Ala Arg Glu Ala Ala Leu Lys  
                     450                      455                      460  
 Ala Gln Ser Glu Arg Lys Pro Gly Gly Glu Arg Glu Glu Arg Gly Lys  
 465                      470                      475                      480  
 Leu Pro Glu Ser Pro Lys Arg Ala Glu Glu Ile Trp Gln Gln Ser Val  
                     485                      490                      495  
 Ile Gly Asp Tyr Leu Ala Arg Phe Lys Asn Asp Arg Val Lys Ala Leu  
                     500                      505                      510  
 Lys Ala Met Glu Met Thr Trp Asn Asn Met Glu Lys Lys Glu Lys Leu  
                     515                      520                      525  
 Met Trp Ile Lys Lys Ala Ala Glu Asp Gln Lys Arg Tyr Glu Arg Glu  
                     530                      535                      540  
 Leu Ser Glu Met Arg Ala Pro Pro Ala Ala Thr Asn Ser Ser Lys Lys  
 545                      550                      555                      560  
 Met Lys Phe Gln Gly Glu Pro Lys Lys Pro Pro Met Asn Gly Tyr Gln  
                     565                      570                      575  
 Lys Phe Ser Gln Glu Leu Leu Ser Asn Gly Glu Leu Asn His Leu Pro  
                     580                      585                      590  
 Leu Lys Glu Arg Met Val Glu Ile Gly Ser Arg Trp Gln Arg Ile Ser  
                     595                      600                      605  
 Gln Ser Gln Lys Glu His Tyr Lys Lys Leu Ala Glu Glu Gln Gln Lys  
                     610                      615                      620  
 Gln Tyr Lys Val His Leu Asp Leu Trp Val Lys Ser Leu Ser Pro Gln  
 625                      630                      635                      640  
 Asp Arg Ala Ala Tyr Lys Glu Tyr Ile Ser Asn Lys Arg Lys Ser Met  
                     645                      650                      655  
 Thr Lys Leu Arg Gly Pro Asn Pro Lys Ser Ser Arg Thr Thr Leu Gln  
                     660                      665                      670

Ser Lys Ser Glu Ser Glu Glu Asp Asp Glu Glu Asp Glu Asp Asp Glu  
 675 680 685

Asp Glu Asp Glu Glu Glu Glu Asp Asp Glu Asn Gly Asp Ser Ser Glu  
 690 695 700

Asp Gly Gly Asp Ser Ser Glu Ser Ser Ser Glu Asp Glu Ser Glu Asp  
 705 710 715 720

Gly Asp Glu Asn Glu Glu Asp Asp Glu Asp Glu Asp Asp Asp Glu Asp  
 725 730 735

Asp Asp Glu Asp Glu Asp Asn Glu Ser Glu Gly Ser Ser Ser Ser Ser  
 740 745 750

Ser Ser Leu Gly Asp Ser Ser Asp Phe Asp Ser Asn  
 755 760

<210> 68  
 <211> 434  
 <212> DNA  
 <213> Homo sapiens

<400> 68  
 ctaagatgct ggatgctgaa gacatcgctg gaactgcccg gccagatgag aaagccatta 60  
 tgacttatgt gtctagcttc tatcatgcct tctctggagc ccagaaggca gaaacagcag 120  
 ccaatcgcat ctgcaaagtg ttggcgggtca atcaagagaa cgagcagctt atggaagact 180  
 atgagaagct ggccagtgat ctgttggagt ggatccgccc caccatccca tggctggaga 240  
 atcgggtgcc tgagaacacc atgcatgcca tgcagcagaa gctggaggac ttccgagact 300  
 atagacgcct gcacaagccg cccaagggtc aggagaagtg ccagctggag atcaacttta 360  
 acacgctgca gaccaaactg cggctcagca accggcctgc cttcatgccc tccgagggca 420  
 ggatgggtctc ggat 434

<210> 69  
 <211> 244  
 <212> DNA  
 <213> Homo sapiens

<400> 69  
 aggcagcatg ctcgttgaga gtcatcacca ctccctaata tcaagtacgc agggacacaa 60  
 acactgcgga aggccgcagg gtcctctgcc taggaaaacc agagaccttt gttcacttgt 120  
 ttatgtgctg accttcctc cactattgtc ctgtgaccct gccaaatccc cctttgtgag 180  
 aaacacccaa gaatgatcaa taaaaataa attaatttag gaaaaaaaaa aaaaaaaact 240  
 cgag 244

<210> 70  
 <211> 437  
 <212> DNA  
 <213> Homo sapiens

<400> 70  
 ctgggacggg agcgtccagc gggactcgaa ccccagatgt gaaggcgttt ctggaaagtc 60  
 cttggctcct ggatccagcg tcggccagcc cagagcccgt gccgcacatc cttgcgtcct 120



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ccaggcagtg ggacccccgc agctgcacgt ccctgggcac ggacaagtgt gaggcactgt 180
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cgtggccccc aggccggagt cttcctaagg ctgtgaggcc acccctgtcc tggcctccgt 300
tctgcagca gcagacctg cccgtgatga gcggggaggc ccttggtctg ctgggccagg 360
ctggttccct ggccatgggg gctgcacctc tgggggagcc agccaaggag gaccccatgc 420
tggcgcagga agccggg 437

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<210> 71  
 <211> 271  
 <212> DNA  
 <213> Homo sapiens

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<400> 71
gctcagagtt ctgtcgtcca ccatcgagt aggaagagag cattggttcc cctgagatag 60
aagagatggc tctcttcagt gccagtcctc catacattaa cccgatcatc ccttttactg 120
gaccaatcca aggagggtg caggaggac ttcagggtgac cctccagggg actaccgaga 180
gttttgacaa aaagtgtgtg gtgaactttt cagaacagct tcaatggaga tgacttgccc 240
ttccacttca accccggtta tgaggaagga g 271

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<210> 72  
 <211> 290  
 <212> DNA  
 <213> Homo sapiens

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<400> 72
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ctggtgcctt ctcctgctgc gaggactcgg cccagggctc gggcccgccc aaggcccta 120
cgttgcccca gggcccagc tctgccttc gccggaacgt gatcagcgag agggagcgca 180
ggaagcggat gtcgttgagc tgtgagcgtc tgcgggccct gctgccccag ttcgatggcc 240
ggcgggagga catggcctcg gtcctggaga tgtctgttgc aattcctgcg 290

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<210> 73  
 <211> 144  
 <212> PRT  
 <213> Homo sapiens

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<400> 73
Lys Met Leu Asp Ala Glu Asp Ile Val Gly Thr Ala Arg Pro Asp Glu
  1           5           10          15
Lys Ala Ile Met Thr Tyr Val Ser Ser Phe Tyr His Ala Phe Ser Gly
          20           25           30
Ala Gln Lys Ala Glu Thr Ala Ala Asn Arg Ile Cys Lys Val Leu Ala
          35           40           45
Val Asn Gln Glu Asn Glu Gln Leu Met Glu Asp Tyr Glu Lys Leu Ala
          50           55           60
Ser Asp Leu Leu Glu Trp Ile Arg Arg Thr Ile Pro Trp Leu Glu Asn
          65           70           75           80
Arg Val Pro Glu Asn Thr Met His Ala Met Gln Gln Lys Leu Glu Asp
          85           90           95

```

Phe Arg Asp Tyr Arg Arg Leu His Lys Pro Pro Lys Val Gln Glu Lys  
 100 105 110

Cys Gln Leu Glu Ile Asn Phe Asn Thr Leu Gln Thr Lys Leu Arg Leu  
 115 120 125

Ser Asn Arg Pro Ala Phe Met Pro Ser Glu Gly Arg Met Val Ser Asp  
 130 135 140

<210> 74

<211> 64

<212> PRT

<213> Homo sapiens

<400> 74

Gly Ser Met Leu Val Glu Ser His His His Ser Leu Ile Ser Ser Thr  
 1 5 10 15

Gln Gly His Lys His Cys Gly Arg Pro Gln Gly Pro Leu Pro Arg Lys  
 20 25 30

Thr Arg Asp Leu Cys Ser Leu Val Tyr Val Leu Thr Phe Pro Pro Leu  
 35 40 45

Leu Ser Cys Asp Pro Ala Lys Ser Pro Phe Val Arg Asn Thr Gln Glu  
 50 55 60

<210> 75

<211> 145

<212> PRT

<213> Homo sapiens

<400> 75

Gly Thr Gly Ala Ser Ser Gly Thr Arg Thr Pro Asp Val Lys Ala Phe  
 1 5 10 15

Leu Glu Ser Pro Trp Ser Leu Asp Pro Ala Ser Ala Ser Pro Glu Pro  
 20 25 30

Val Pro His Ile Leu Ala Ser Ser Arg Gln Trp Asp Pro Ala Ser Cys  
 35 40 45

Thr Ser Leu Gly Thr Asp Lys Cys Glu Ala Leu Leu Gly Leu Cys Gln  
 50 55 60

Val Arg Gly Gly Leu Pro Pro Phe Ser Glu Pro Ser Ser Leu Val Pro  
 65 70 75 80

Trp Pro Pro Gly Arg Ser Leu Pro Lys Ala Val Arg Pro Pro Leu Ser  
 85 90 95

Trp Pro Pro Phe Ser Gln Gln Gln Thr Leu Pro Val Met Ser Gly Glu  
 100 105 110

Ala Leu Gly Trp Leu Gly Gln Ala Gly Ser Leu Ala Met Gly Ala Ala  
115 120 125

Pro Leu Gly Glu Pro Ala Lys Glu Asp Pro Met Leu Ala Gln Glu Ala  
130 135 140

Gly  
145

<210> 76  
<211> 69  
<212> PRT  
<213> Homo sapiens

<400> 76  
Ala Glu Phe Cys Arg Pro Pro Ser Ser Glu Glu Glu Ser Ile Gly Ser  
1 5 10 15

Pro Glu Ile Glu Glu Met Ala Leu Phe Ser Ala Gln Ser Pro Tyr Ile  
20 25 30

Asn Pro Ile Ile Pro Phe Thr Gly Pro Ile Gln Gly Gly Leu Gln Glu  
35 40 45

Gly Leu Gln Val Thr Leu Gln Gly Thr Thr Glu Ser Phe Ala Gln Lys  
50 55 60

Phe Val Val Asn Phe  
65

<210> 77  
<211> 96  
<212> PRT  
<213> Homo sapiens

<400> 77  
Glu Pro Tyr Pro Glu Val Ser Arg Ile Pro Thr Val Arg Gly Cys Asn  
1 5 10 15

Gly Ser Leu Ser Gly Ala Leu Ser Cys Cys Glu Asp Ser Ala Gln Gly  
20 25 30

Ser Gly Pro Pro Lys Ala Pro Thr Val Ala Glu Gly Pro Ser Ser Cys  
35 40 45

Leu Arg Arg Asn Val Ile Ser Glu Arg Glu Arg Arg Lys Arg Met Ser  
50 55 60

Leu Ser Cys Glu Arg Leu Arg Ala Leu Leu Pro Gln Phe Asp Gly Arg  
65 70 75 80

Arg Glu Asp Met Ala Ser Val Leu Glu Met Ser Val Ala Ile Pro Ala

85

90

95

<210> 78  
 <211> 2076  
 <212> DNA  
 <213> Homo sapiens

<400> 78  
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 aggaaataga agttgcccc ccaaagacta aagaagttcg cattaagatt ttggccacag 180  
 gaatctgtcg cacagatgac catgtgataa aaggaacaat ggtgtccaag tttccagtga 240  
 ttgtgggaca tgaggcaact gggattgtag agagcattgg agaaggagtg actacagtga 300  
 aaccagggtga caaagtcac cctctctttc tgccacaatg tagagaatgc aatgcttgtc 360  
 gcaacccaga tggcaacctt tgcattagga gcgataattc tggctgtgga gtactggctg 420  
 atggcaccac cagatttaca tgcaagggca aaccagtcca ccacttcag aacaccagta 480  
 catttaccga gtacacagtg gtggatgaat ctctctgtgc taagattgat gatgcagctc 540  
 ctcttgagaa agtctgttta attggctgtg ggttttccac tggatatggc gctgctgtta 600  
 aaaactggcaa ggtcaaacct ggttccactt gcgtcgtctt tggcctgaga ggagtggcc 660  
 ttgcagtcac catgggctgt aagtcagctg gtgcatttag gatcattggg attgacctca 720  
 acaaaagacaa atttgagaag gccatggctg taggtgccac tgagtgtatc agtcccaagg 780  
 actctaccaa acccatcagt gaggtgctgt cagaaatgac aggcaacaac gtgggatata 840  
 cctttgaagt tattgggcat cttgaaacca tgattgatgc cctggcatcc tgccacatga 900  
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 cgatgttgct cttcactgga cgcacatgga agggatgtgt ctttggaggt ttgaaaagca 1020  
 gagatgatgt cccaaaacta gtgactgagt tcctggcaaa gaaatttgac ctggaccagt 1080  
 tgataactca tgtcttacca tttaaaaaaa tcagtgaagg atttgagctg ctcaattcag 1140  
 gacaaagcat tcgaacggtc ctgacgtttt gagatccaaa gtggcaggag gtctgtgttg 1200  
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 aatatttttg atttacattt tgtaaggcta taattgtatc ttttaagaaa acatacactt 1440  
 ggatttctat gttgaaatgg agatttttaa gagttttaac cagctgctgc agatatatat 1500  
 ctcaaaacag atatagcgtg taaagatata gtaaatgcat ctctagagt aatattcact 1560  
 taacacattg aaactattat tttttagatt tgaatataaa tgtatttttt aaacacttgt 1620  
 tatgagttaa cttggattac attttgaaat cagttcattc catgatgcat attactggat 1680  
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 tcattacata acttggtgaa actgaaaaag tatatcatat gggtagacaa ggctatttgc 1800  
 cagcatatat taatatttta gaaaatattc cttttgtaat actgaatata aacatagagc 1860  
 tagaatcata ttatcatact tatcataatg ttcaatttga tacagtagaa ttgcaagtc 1920  
 ttaagtcctt attcactgtg cttagtagtg actccattta ataaaaagt tttttagttt 1980  
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 ttaaaaatta tataaaaaaa aaaaaaaaaa ctcgag 2076

<210> 79  
 <211> 2790  
 <212> DNA  
 <213> Homo sapiens

<400> 79  
 aagcagttga gtaggcagaa aaaagaacct cttcattaag gattaaaatg tataggccag 60  
 cacgtgtaac ttcgacttca agatttctga atccatattg agtatgtttc attgtcgtcg 120  
 caggggtagt gatcctggca gtcaccatag ctctacttgt ttacttttta gcttttgatc 180  
 aaaaatctta cttttatagg agcagttttc aactcctaaa tgttgaatat aatagtcagt 240

taaattcacc agctacacag gaatacagga ctttgagtgg aagaattgaa tctctgatta 300  
ctaaaacatt caaagaatca aatttaagaa atcagttcat cagagctcat gttgccaaac 360  
tgaggcaaga tggtagtggg gtgagagcgg atgttgatcat gaaatttcaa ttcactagaa 420  
ataacaatgg agcatcaatg aaaagcagaa ttgagtctgt tttacgacaa atgctgaata 480  
actctggaaa cctggaaata aaccttcaa ctgagataac atcacttact gaccaggctg 540  
cagcaaattg gcttattaat gaatgtgggg ccggtccaga cctaataaca ttgtctgagc 600  
agagaatcct tggaggcact gaggctgagg aggggaagctg gccgtggcaa gtcagctgc 660  
ggctcaataa tgcccaccac tgtggaggca gcttgatcaa taacatgtgg atcctgacag 720  
cagctcactg cttcagaagc aactctaate ctcgtgactg gattgccacg tctggtattt 780  
ccacaacatt tcctaaacta agaagtagag taagaaatat ttttaattcat aacaattata 840  
aatctgcaac tcatgaaaat gacattgcac ttgtgagact tgagaacagt gtcacattta 900  
ccaaagatat ccatagtgtg tgtctcccag ctgctacca gaattattca cctggctcta 960  
ctgcttatgt aacaggatgg ggcgtcaag aatatgctgg ccacacagtt ccagagctaa 1020  
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gagccatctt gtctggaatg ctgtgtgctg gtagacctca aggtggagtg gacgcatgtc 1140  
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ctgttgcaaa gtctgtatgc aggtgtgcct gtcttaaat ccaaagcttt acatttcaac 1380  
tgaaaaagaa actagaaatg tcctaattta acatcttgtt acataaatat ggtttaacaa 1440  
acactgttta acctttcttt attattaaag gttttctatt ttctccagag aactatatga 1500  
atgttgcata gtactgtggc tgtgtaacag aagaaacaca ctaaaactaat tacaaggtta 1560  
acaatttcat tacagttgtg ctaaaagccc gtagtgagaa gaacaggaaac cttgagcatg 1620  
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aggatgagaa gtaagcaaac tgtggaaaca tgcaaaggaa aaagtgatag aataatattc 1740  
aagacaaaaa gaacagtatg aggcaagaga aatagtatgt atttaaaatt tttggttact 1800  
caatatctta tacttagtat gtagctctaa attaaaaatg tgaaactgtt gtactatacg 1860  
tataacctaa ccttaattat tctgtaagaa catgcttcca taggaaatag tggataattt 1920  
tcagctattt aaggcaaaa ctaaaatagt tcaactctca actgagacc aaagaattat 1980  
agatattttt catgatgacc catgaaaaat atcactcatc tacataaagg agagactata 2040  
tctattttat agagaagcta agaaatatac ctacacaaac ttgtcaggtg ctttacaact 2100  
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gtcactcttc ctctctcatt ttctttctct ctctctcccc ttctcatata catgctctcc 2400  
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gcaaacacct acaataaagc catctacttt tagggaaagg gagttgaaa tgcaaccaac 2700  
tcttggcgaa ctgtacaaac aaatctttgc tatactttat ttcaaataa ttctttttga 2760  
aatgaaaaaa aaaaaaaaaa aaactcgag 2790

&lt;210&gt; 80

&lt;211&gt; 1460

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 80

ctcaaagcag ttgagtaggc agaaaaaaga acctcttcat taaggattaa aatgtatagg 60  
ccagcacgtg taacttcgac ttcaagattt ctgaatccat atgtagtatg tttcattgtc 120  
gtcgcagggg tagtgatcct ggcagtcacc atagctctac ttgtttactt tttagctttt 180  
gatcaaaaat cttactttta taggagcagt tttaactcc taaatgttga atataatagt 240  
cagttaaatt caccagctac acaggaatac aggactttga gtggaagaat tgaatctctg 300

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attactaaaa cattcaaaga atcaaattta agaaatcagt tcatcagagc tcatgttgcc 360
aaactgaggc aagatggttag tgggtgtgaga gcggatgttg tcatgaaatt tcaattcact 420
agaaataaca atggagcatc aatgaaaagc agaattgagt ctgttttacg acaaatgctg 480
aataactctg gaaacctgga aataaacctt tcaactgaga taacatcact tactgaccag 540
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gagcagagaa tccttggagg cactgaggct gaggaggga gctggccgtg gcaagtcagt 660
ctgcccgtca ataatgccc cactgtgga ggcagcctga tcaataacat gtggatcctg 720
acagcagctc actgtttcag aagcaactct aatcctcgtg actggattgc cagctctggt 780
atttccacaa catttcctaa actaagaatg agagtaagaa atattttaat tcataacaat 840
tataaatctg caactcatga aatgacatt gcacttgtga gacttgagaa cagtgtcacc 900
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caactgaaaa agaaactaga aatgtcctaa tttaacatct tgttacataa atatggttta 1440
acaaaaaaaa aaaaaaaaaa 1460

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&lt;210&gt; 81

&lt;211&gt; 386

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 81

Met Phe Ala Glu Ile Gln Ile Gln Asp Lys Asp Arg Met Gly Thr Ala  
1 5 10 15

Gly Lys Val Ile Lys Cys Lys Ala Ala Val Leu Trp Glu Gln Lys Gln  
20 25 30

Pro Phe Ser Ile Glu Glu Ile Glu Val Ala Pro Pro Lys Thr Lys Glu  
35 40 45

Val Arg Ile Lys Ile Leu Ala Thr Gly Ile Cys Arg Thr Asp Asp His  
50 55 60

Val Ile Lys Gly Thr Met Val Ser Lys Phe Pro Val Ile Val Gly His  
65 70 75 80

Glu Ala Thr Gly Ile Val Glu Ser Ile Gly Glu Gly Val Thr Thr Val  
85 90 95

Lys Pro Gly Asp Lys Val Ile Pro Leu Phe Leu Pro Gln Cys Arg Glu  
100 105 110

Cys Asn Ala Cys Arg Asn Pro Asp Gly Asn Leu Cys Ile Arg Ser Asp  
115 120 125

Ile Thr Gly Arg Gly Val Leu Ala Asp Gly Thr Thr Arg Phe Thr Cys  
130 135 140

Lys Gly Lys Pro Val His His Phe Met Asn Thr Ser Thr Phe Thr Glu

145                      150                      155                      160  
 Tyr Thr Val Val Asp Glu Ser Ser Val Ala Lys Ile Asp Asp Ala Ala  
                                  165                                   170                                   175  
 Pro Pro Glu Lys Val Cys Leu Ile Gly Cys Gly Phe Ser Thr Gly Tyr  
                                  180                                   185                                   190  
 Gly Ala Ala Val Lys Thr Gly Lys Val Lys Pro Gly Ser Thr Cys Val  
                                  195                                   200                                   205  
 Val Phe Gly Leu Arg Gly Val Gly Leu Ser Val Ile Met Gly Cys Lys  
                                  210                                   215                                   220  
 Ser Ala Gly Ala Ser Arg Ile Ile Gly Ile Asp Leu Asn Lys Asp Lys  
                                  225                                   230                                   235                                   240  
 Phe Glu Lys Ala Met Ala Val Gly Ala Thr Glu Cys Ile Ser Pro Lys  
                                  245                                   250                                   255  
 Asp Ser Thr Lys Pro Ile Ser Glu Val Leu Ser Glu Met Thr Gly Asn  
                                  260                                   265                                   270  
 Asn Val Gly Tyr Thr Phe Glu Val Ile Gly His Leu Glu Thr Met Ile  
                                  275                                   280                                   285  
 Asp Ala Leu Ala Ser Cys His Met Asn Tyr Gly Thr Ser Val Val Val  
                                  290                                   295                                   300  
 Gly Val Pro Pro Ser Ala Lys Met Leu Thr Tyr Asp Pro Met Leu Leu  
                                  305                                   310                                   315                                   320  
 Phe Thr Gly Arg Thr Trp Lys Gly Cys Val Phe Gly Gly Leu Lys Ser  
                                  325                                   330                                   335  
 Arg Asp Asp Val Pro Lys Leu Val Thr Glu Phe Leu Ala Lys Lys Phe  
                                  340                                   345                                   350  
 Asp Leu Asp Gln Leu Ile Thr His Val Leu Pro Phe Lys Lys Ile Ser  
                                  355                                   360                                   365  
 Glu Gly Phe Glu Leu Leu Asn Ser Gly Gln Ser Ile Arg Thr Val Leu  
                                  370                                   375                                   380  
 Thr Phe  
 385

&lt;210&gt; 82

&lt;211&gt; 418

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 82

Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro

1	5	10	15
Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val	20	25	30
Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr	35	40	45
Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln	50	55	60
Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile	65	70	75
Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln	85	90	95
Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val	100	105	110
Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly	115	120	125
Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn	130	135	140
Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu	145	150	155
Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly	165	170	175
Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu	180	185	190
Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn	195	200	205
Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr	210	215	220
Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala	225	230	235
Thr Ser Gly Ile Ser Thr Thr Phe Pro Lys Leu Arg Met Arg Val Arg	245	250	255
Asn Ile Leu Ile His Asn Asn Tyr Lys Ser Ala Thr His Glu Asn Asp	260	265	270
Ile Ala Leu Val Arg Leu Glu Asn Ser Val Thr Phe Thr Lys Asp Ile	275	280	285
His Ser Val Cys Leu Pro Ala Ala Thr Gln Asn Ile Pro Pro Gly Ser	290	295	300



Thr Ala Tyr Val Thr Gly Trp Gly Ala Gln Glu Tyr Ala Gly His Thr  
305 310 315 320

Val Pro Glu Leu Arg Gln Gly Gln Val Arg Ile Ile Ser Asn Asp Val  
325 330 335

Cys Asn Ala Pro His Ser Tyr Asn Gly Ala Ile Leu Ser Gly Met Leu  
340 345 350

Cys Ala Gly Val Pro Gln Gly Gly Val Asp Ala Cys Gln Gly Asp Ser  
355 360 365

Gly Gly Pro Leu Val Gln Glu Asp Ser Arg Arg Leu Trp Phe Ile Val  
370 375 380

Gly Ile Val Ser Trp Gly Asp Gln Cys Gly Leu Pro Asp Lys Pro Gly  
385 390 395 400

Val Tyr Thr Arg Val Thr Ala Tyr Leu Asp Trp Ile Arg Gln Gln Thr  
405 410 415

Gly Ile

<210> 83

<211> 418

<212> PRT

<213> Homo sapiens

<400> 83

Met Tyr Arg Pro Ala Arg Val Thr Ser Thr Ser Arg Phe Leu Asn Pro  
1 5 10 15

Tyr Val Val Cys Phe Ile Val Val Ala Gly Val Val Ile Leu Ala Val  
20 25 30

Thr Ile Ala Leu Leu Val Tyr Phe Leu Ala Phe Asp Gln Lys Ser Tyr  
35 40 45

Phe Tyr Arg Ser Ser Phe Gln Leu Leu Asn Val Glu Tyr Asn Ser Gln  
50 55 60

Leu Asn Ser Pro Ala Thr Gln Glu Tyr Arg Thr Leu Ser Gly Arg Ile  
65 70 75 80

Glu Ser Leu Ile Thr Lys Thr Phe Lys Glu Ser Asn Leu Arg Asn Gln  
85 90 95

Phe Ile Arg Ala His Val Ala Lys Leu Arg Gln Asp Gly Ser Gly Val  
100 105 110

Arg Ala Asp Val Val Met Lys Phe Gln Phe Thr Arg Asn Asn Asn Gly  
115 120 125

Ala Ser Met Lys Ser Arg Ile Glu Ser Val Leu Arg Gln Met Leu Asn  
130 135 140

Asn Ser Gly Asn Leu Glu Ile Asn Pro Ser Thr Glu Ile Thr Ser Leu  
145 150 155 160

Thr Asp Gln Ala Ala Ala Asn Trp Leu Ile Asn Glu Cys Gly Ala Gly  
165 170 175

Pro Asp Leu Ile Thr Leu Ser Glu Gln Arg Ile Leu Gly Gly Thr Glu  
180 185 190

Ala Glu Glu Gly Ser Trp Pro Trp Gln Val Ser Leu Arg Leu Asn Asn  
195 200 205

Ala His His Cys Gly Gly Ser Leu Ile Asn Asn Met Trp Ile Leu Thr  
210 215 220

Ala Ala His Cys Phe Arg Ser Asn Ser Asn Pro Arg Asp Trp Ile Ala  
225 230 235 240

Thr Ser Gly Ile Ser Thr Thr Phe Pro Lys Leu Arg Met Arg Val Arg  
245 250 255

Asn Ile Leu Ile His Asn Asn Tyr Lys Ser Ala Thr His Glu Asn Asp  
260 265 270

Ile Ala Leu Val Arg Leu Glu Asn Ser Val Thr Phe Thr Lys Asp Ile  
275 280 285

His Ser Val Cys Leu Pro Ala Ala Thr Gln Asn Ile Pro Pro Gly Ser  
290 295 300

Thr Ala Tyr Val Thr Gly Trp Gly Ala Gln Glu Tyr Ala Gly His Thr  
305 310 315 320

Val Pro Glu Leu Arg Gln Gly Gln Val Arg Ile Ile Ser Asn Asp Val  
325 330 335

Cys Asn Ala Pro His Ser Tyr Asn Gly Ala Ile Leu Ser Gly Met Leu  
340 345 350

Cys Ala Gly Val Pro Gln Gly Gly Val Asp Ala Cys Gln Gly Asp Ser  
355 360 365

Gly Gly Pro Leu Val Gln Glu Asp Ser Arg Arg Leu Trp Phe Ile Val  
370 375 380

Gly Ile Val Ser Trp Gly Asp Gln Cys Gly Leu Pro Asp Lys Pro Gly  
385 390 395 400

Val Tyr Thr Arg Val Thr Ala Tyr Leu Asp Trp Ile Arg Gln Gln Thr  
405 410 415

## Gly Ile

&lt;210&gt; 84

&lt;211&gt; 489

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 84

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aattacagag gagtttcatg gcactaagtc aagatattca gaaaacaata aagaagacag 180  
cacgtcggga gcagcttatg agagaagaag ctgaacagaa acgtttaaaa actgtacttg 240  
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gtttgaatgg agtgccaata ttgtccgaag aggagttgtc attgttggat gaattctata 360  
agctagtaga ccctgaacgg gacatgagct tgaggttgga tgaacagtat gaacatgcct 420  
ccattcacct gtgggacctg ctggaaggga aggaaaaacc tgtatgtgga accacctata 480  
aagttctaa 489

&lt;210&gt; 85

&lt;211&gt; 304

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 85

gggacctgga ggaggccacg ctgcagcatg aagccacagc agccaccctg aggaagaagc 60  
acgcggacag cgtggccgag ctgggggagc agatcgacaa cctgcagcgg gtgaagcaga 120  
agctggagaa ggagaagagc gagatgaaga tggagatcga tgacctcgct tgtaacatgg 180  
aggatcatctc caaatctaag ggaaaccttg agaagatgtg ccgcacactg gaggaccaag 240  
tgagtgaact gaagaccagc gaggaggaac agcagcggct gatcaatgaa ctgactgcgc 300  
agag 304

&lt;210&gt; 86

&lt;211&gt; 296

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 86

gaaaatcctt cctttgaatg ggaatctcca agcagttgaa ttgggcgaaa aaagaacctc 60  
ttccttaagg attaaaaatgt ttagggcaac acgtgttact tccacttcca gatttctgaa 120  
tccatatgtt gtatgtttcc ttgtcctccc aggggttgtg atcctggcag tccccatagc 180  
tctacttgtt tacttttttag cttttgatca aaaatcttac ttttattgga gcaattttcc 240  
actcccaaat gttgaatata atagtccgtt taattcccc gcttcaccgg gaattc 296

&lt;210&gt; 87

&lt;211&gt; 904

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 87

gtgtccagga aacgattcat gaacataaca agcttgctgc aaattcagat catctcatgc 60  
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tatctgatcg ttctaaaaaa gagttgtccc cggttttaac cagtgaagtt catagtgttc 180  
gtgcaggacg gcatcttgct accaaattga atattttagt acagcaacat tttgacttgg 240  
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gttctgtttt attggaacaa ccacgaaagt caggttctaa agtcattagt catatgctta 600  
gtagccatgg aggagagatt tttttgcacg tccttagcag ttctcgatcc attctagaag 660  
atccaccttc aattagtga ggaatgtggag gaagagttac agactaccgg attacagatt 720  
ttggtgaatt tatgagggga aaacagatta actccttttc tacaccccag atataaaatc 780  
gatggaagtc ttgaggtccc tttggaaccg agccaaaaga tcagttaaaa aaacataccc 840  
gttactggcc tatgatttca aaaaccacc atttttaaca tgcaagcggg agttccgtta 900  
acca 904

&lt;210&gt; 88

&lt;211&gt; 387

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 88

cgtctctccc ccagtttgcc gttcaccccg agcgcctcggg acttgccgat agtggtgacg 60  
gcggaacat gtctgtggct ttcgcggccc cgaggcagcg aggcaagggg gagatcactc 120  
ccgctgcgat tcagaagatg ttggatgaca ataaccatct tattcagtgt ataaggact 180  
ctcagaataa aggaaagacc tcagagtgtt ctcagtatca gcagatgttg cacacaaact 240  
tggtatacct tgctacaata gcagattcta atcaaaatat gcagtctctt ttaccagcac 300  
caccacaca gaatatgcct atgggtcctg gagggatgaa tcagagcggg cttccccac 360  
ctccacgctc tcacaacatg cttcaa 387

&lt;210&gt; 89

&lt;211&gt; 481

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 89

tggtcttgga cctgcgggtgc tatagagcag gctcttctag gttggcagtt gccatggaat 60  
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atgtggaaaa gggtagacct aagaatgact cctggatctt tgccctggct gtgctectgt 420  
gcagcacctt tgtctacaac agcatgagca ccatcaacca ccaggccctg gagcagctgc 480  
a 481

&lt;210&gt; 90

&lt;211&gt; 491

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 90

tgaaaactgt tcttggaact gcggtgctat agagcaggtt ggcagttgcc atggaatctg 60  
gacccaaaat gttggcccc gtttgccctg tggaaaataa caatgagcag ctattggtga 120  
accagcaagc tatacagatt cttgaaaaga tttctcagcc agtgggtgggtg gtggccattg 180  
taggactgta ccgtacaggg aaatcctact tgatgaacca tctggcagga cagaatcatg 240  
gttccctctt gggtccacg gtgcagctctg aaaccaaggg catctggatg tgggtcgtgc 300  
cccaccatc caagccaaac cacaccctgg tccttctgga caccgaaggt ctgggcatg 360  
tggaaaaggg tgaccctaag aatgactcct ggatctttgc cctggctgtg ctctgtgca 420  
gcacctttgt ctacaacagc atgagcacca tcaaccacca agccctggag cagctgcatt 480

atgtgacgga c

491

&lt;210&gt; 91

&lt;211&gt; 488

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 91

ttcgacagtc agccgcatct tcttttgcgt cgccagccga gccacatcgc tcagacacca 60  
 tggggaaggt gaaggtcgga gtcaacggat ttggtcgat tgggcgctg gtcaccagg 120  
 ctgcttttaa ctctggtaaa gtggatattg ttgccatcaa tgacccttc attgacctca 180  
 actacatggt ttacatgttc caatatgatt ccacccatgg caaattccat ggcaccgtcg 240  
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 atccctccaa aatcaagtgg ggcgatgctg gcgctgagta cgtcgtggag tccactggcg 360  
 tcttcaccac catggagaag gctggggctc atttgcaggg gggagccaaa agggcatca 420  
 tctctgcccc tctgctgatg ccccatgttc gtcatgggtg tgaaccatga gaagtatgac 480  
 acagcctc 488

&lt;210&gt; 92

&lt;211&gt; 384

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 92

gacagtcagc cgcattctct tttgcgtcgc cagccgagcc acatcgctca gacaccatgg 60  
 ggaaggtgaa ggtcggagtc aacggatttg gtcgtattgg gcgctggtc accagggctg 120  
 cttttaactc tggtaaagtg gatattgttg ccatcaatga ccccttcatt gacctcaact 180  
 acatggttta catgttccaa tatgattcca cccatggcaa attccatggc accgtcgagg 240  
 ctgagaacgg gaagcttgtc atcaatggaa atcccatcac catcttccag gacgcgagtc 300  
 cctccaaaat caagtggggc gatactggcg ctgagtacgt cgtggagtcc actggcgctc 360  
 tcaccaccat ggagaaggct gggg 384

&lt;210&gt; 93

&lt;211&gt; 162

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 93

Lys Gly Lys Leu Asp Asp Tyr Gln Glu Arg Met Asn Lys Gly Glu Arg  
 1 5 10 15  
 Leu Asn Gln Asp Gln Leu Asp Ala Val Ser Lys Tyr Gln Glu Val Thr  
 20 25 30  
 Asn Asn Leu Glu Phe Ala Lys Glu Leu Gln Arg Ser Phe Met Ala Leu  
 35 40 45  
 Ser Gln Asp Ile Gln Lys Thr Ile Lys Lys Thr Ala Arg Arg Glu Gln  
 50 55 60  
 Leu Met Arg Glu Glu Ala Glu Gln Lys Arg Leu Lys Thr Val Leu Glu  
 65 70 75 80  
 Leu Gln Tyr Val Leu Asp Lys Leu Gly Asp Asp Glu Val Arg Thr Asp  
 85 90 95

Leu Lys Gln Gly Leu Asn Gly Val Pro Ile Leu Ser Glu Glu Glu Leu  
100 105 110

Ser Leu Leu Asp Glu Phe Tyr Lys Leu Val Asp Pro Glu Arg Asp Met  
115 120 125

Ser Leu Arg Leu Asn Glu Gln Tyr Glu His Ala Ser Ile His Leu Trp  
130 135 140

Asp Leu Leu Glu Gly Lys Glu Lys Pro Val Cys Gly Thr Thr Tyr Lys  
145 150 155 160

Val Leu

<210> 94

<211> 100

<212> PRT

<213> Homo sapiens

<400> 94

Asp Leu Glu Glu Ala Thr Leu Gln His Glu Ala Thr Ala Ala Thr Leu  
1 5 10 15

Arg Lys Lys His Ala Asp Ser Val Ala Glu Leu Gly Glu Gln Ile Asp  
20 25 30

Asn Leu Gln Arg Val Lys Gln Lys Leu Glu Lys Glu Lys Ser Glu Met  
35 40 45

~~Lys Met Glu Ile Asp Asp Leu Ala Cys Asn Met Glu Val Ile Ser Lys~~  
50 55 60

Ser Lys Gly Asn Leu Glu Lys Met Cys Arg Thr Leu Glu Asp Gln Val  
65 70 75 80

Ser Glu Leu Lys Thr Gln Glu Glu Glu Gln Gln Arg Leu Ile Asn Glu  
85 90 95

Leu Thr Ala Gln  
100

<210> 95

<211> 99

<212> PRT

<213> Homo sapiens

<400> 95

Lys Ile Leu Pro Leu Asn Gly Asn Leu Gln Ala Val Glu Leu Gly Glu  
1 5 10 15

Lys Arg Thr Ser Ser Leu Arg Ile Lys Met Phe Arg Ala Thr Arg Val  
20 25 30

Thr Ser Thr Ser Arg Phe Leu Asn Pro Tyr Val Val Cys Phe Leu Val  
35 40 45

Leu Pro Gly Val Val Ile Leu Ala Val Pro Ile Ala Leu Leu Val Tyr  
50 55 60

Phe Leu Ala Phe Asp Gln Lys Ser Tyr Phe Tyr Trp Ser Asn Phe Pro  
65 70 75 80

Leu Pro Asn Val Glu Tyr Asn Ser Pro Phe Asn Ser Pro Ala Ser Pro  
85 90 95

Gly Ile Pro

<210> 96

<211> 257

<212> PRT

<213> Homo sapiens

<400> 96

Val Gln Glu Thr Ile His Glu His Asn Lys Leu Ala Ala Asn Ser Asp  
1 5 10 15

His Leu Met Gln Ile Gln Lys Cys Glu Leu Val Leu Ile His Thr Tyr  
20 25 30

Pro Val Gly Glu Asp Ser Leu Val Ser Asp Arg Ser Lys Lys Glu Leu  
35 40 45

Ser Pro Val Leu Thr Ser Glu Val His Ser Val Arg Ala Gly Arg His  
50 55 60

Leu Ala Thr Lys Leu Asn Ile Leu Val Gln Gln His Phe Asp Leu Ala  
65 70 75 80

Ser Thr Thr Ile Thr Asn Ile Pro Met Lys Glu Glu Gln His Ala Asn  
85 90 95

Thr Ser Ala Asn Tyr Asp Val Glu Leu Leu His His Lys Asp Ala His  
100 105 110

Val Asp Phe Leu Lys Ser Gly Asp Ser His Leu Gly Gly Gly Ser Arg  
115 120 125

Glu Gly Ser Phe Lys Glu Thr Ile Thr Leu Lys Trp Cys Thr Pro Arg  
130 135 140

Thr Asn Asn Ile Glu Leu His Tyr Cys Thr Gly Ala Tyr Arg Ile Ser  
145 150 155 160

Pro Val Asp Val Asn Ser Arg Pro Ser Ser Cys Leu Thr Asn Phe Leu  
165 170 175

Leu Asn Gly Arg Ser Val Leu Leu Glu Gln Pro Arg Lys Ser Gly Ser  
 180 185 190  
 Lys Val Ile Ser His Met Leu Ser Ser His Gly Gly Glu Ile Phe Leu  
 195 200 205  
 His Val Leu Ser Ser Ser Arg Ser Ile Leu Glu Asp Pro Pro Ser Ile  
 210 215 220  
 Ser Glu Gly Cys Gly Gly Arg Val Thr Asp Tyr Arg Ile Thr Asp Phe  
 225 230 235 240  
 Gly Glu Phe Met Arg Gly Lys Gln Ile Asn Ser Phe Ser Thr Pro Gln  
 245 250 255  
 Ile

<210> 97  
 <211> 128  
 <212> PRT  
 <213> Homo sapiens

<400> 97  
 Ser Leu Pro Gln Phe Ala Val His Pro Glu Arg Ser Gly Leu Ala Asp  
 1 5 10 15  
 Ser Gly Asp Gly Gly Asn Met Ser Val Ala Phe Ala Ala Pro Arg Gln  
 20 25 30  
 Arg Gly Lys Gly Glu Ile Thr Pro Ala Ala Ile Gln Lys Met Leu Asp  
 35 40 45  
 Asp Asn Asn His Leu Ile Gln Cys Ile Met Asp Ser Gln Asn Lys Gly  
 50 55 60  
 Lys Thr Ser Glu Cys Ser Gln Tyr Gln Gln Met Leu His Thr Asn Leu  
 65 70 75 80  
 Val Tyr Leu Ala Thr Ile Ala Asp Ser Asn Gln Asn Met Gln Ser Leu  
 85 90 95  
 Leu Pro Ala Pro Pro Thr Gln Asn Met Pro Met Gly Pro Gly Gly Met  
 100 105 110  
 Asn Gln Ser Gly Pro Pro Pro Pro Arg Ser His Asn Met Pro Ser  
 115 120 125

<210> 98  
 <211> 159  
 <212> PRT  
 <213> Homo sapiens



&lt;400&gt; 98

Phe Leu Asp Leu Arg Cys Tyr Arg Ala Gly Ser Ser Arg Leu Ala Val  
 1 5 10 15  
 Ala Met Glu Ser Gly Pro Lys Met Leu Ala Pro Val Cys Leu Val Glu  
 20 25 30  
 Asn Asn Asn Glu Gln Leu Leu Val Asn Gln Gln Ala Ile Gln Ile Leu  
 35 40 45  
 Glu Lys Ile Ser Gln Pro Val Val Val Ala Ile Val Gly Leu Tyr  
 50 55 60  
 Arg Thr Gly Lys Ser Tyr Leu Met Asn His Leu Ala Gly Gln Asn His  
 65 70 75 80  
 Gly Phe Pro Leu Gly Ser Thr Val Gln Ser Glu Thr Lys Gly Ile Trp  
 85 90 95  
 Met Trp Cys Val Pro His Pro Ser Lys Pro Asn His Thr Leu Val Leu  
 100 105 110  
 Leu Asp Thr Glu Gly Leu Gly Asp Val Glu Lys Gly Asp Pro Lys Asn  
 115 120 125  
 Asp Ser Trp Ile Phe Ala Leu Ala Val Leu Leu Cys Ser Thr Phe Val  
 130 135 140  
 Tyr Asn Ser Met Ser Thr Ile Asn His Gln Ala Leu Glu Gln Leu  
 145 150 155

&lt;210&gt; 99

&lt;211&gt; 147

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 99

Met Glu Ser Gly Pro Lys Met Leu Ala Pro Val Cys Leu Val Glu Asn  
 1 5 10 15  
 Asn Asn Glu Gln Leu Leu Val Asn Gln Gln Ala Ile Gln Ile Leu Glu  
 20 25 30  
 Lys Ile Ser Gln Pro Val Val Val Val Ala Ile Val Gly Leu Tyr Arg  
 35 40 45  
 Thr Gly Lys Ser Tyr Leu Met Asn His Leu Ala Gly Gln Asn His Gly  
 50 55 60  
 Phe Pro Leu Gly Ser Thr Val Gln Ser Glu Thr Lys Gly Ile Trp Met  
 65 70 75 80  
 Trp Cys Val Pro His Pro Ser Lys Pro Asn His Thr Leu Val Leu Leu

85 90 95

Asp Thr Glu Gly Leu Gly Asp Val Glu Lys Gly Asp Pro Lys Asn Asp  
100 105 110

Ser Trp Ile Phe Ala Leu Ala Val Leu Leu Cys Ser Thr Phe Val Tyr  
115 120 125

Asn Ser Met Ser Thr Ile Asn His Gln Ala Leu Glu Gln Leu His Tyr  
130 135 140

Val Thr Asp  
145

<210> 100  
<211> 124  
<212> PRT  
<213> Homo sapiens

<400> 100  
Met Gly Lys Val Lys Val Gly Val Asn Gly Phe Gly Arg Ile Gly Arg  
1 5 10 15  
Leu Val Thr Arg Ala Ala Phe Asn Ser Gly Lys Val Asp Ile Val Ala  
20 25 30  
Ile Asn Asp Pro Phe Ile Asp Leu Asn Tyr Met Val Tyr Met Phe Gln  
35 40 45  
Tyr Asp Ser Thr His Gly Lys Phe His Gly Thr Val Glu Ala Glu Asn  
50 55 60  
Gly Lys Leu Val Ile Asn Gly Asn Pro Ile Thr Ile Phe Gln Glu Arg  
65 70 75 80  
Asp Pro Ser Lys Ile Lys Trp Gly Asp Ala Gly Ala Glu Tyr Val Val  
85 90 95  
Glu Ser Thr Gly Val Phe Thr Thr Met Glu Lys Ala Gly Ala His Leu  
100 105 110  
Gln Gly Gly Ala Lys Arg Val Ile Ile Ser Ala Pro  
115 120

<210> 101  
<211> 127  
<212> PRT  
<213> Homo sapiens

<400> 101  
Gln Ser Ala Ala Ser Ser Phe Ala Ser Pro Ala Glu Pro His Arg Ser  
1 5 10 15

Asp Thr Met Gly Lys Val Lys Val Gly Val Asn Gly Phe Gly Arg Ile  
 20 25 30  
 Gly Arg Leu Val Thr Arg Ala Ala Phe Asn Ser Gly Lys Val Asp Ile  
 35 40 45  
 Val Ala Ile Asn Asp Pro Phe Ile Asp Leu Asn Tyr Met Val Tyr Met  
 50 55 60  
 Phe Gln Tyr Asp Ser Thr His Gly Lys Phe His Gly Thr Val Glu Ala  
 65 70 75 80  
 Glu Asn Gly Lys Leu Val Ile Asn Gly Asn Pro Ile Thr Ile Phe Gln  
 85 90 95  
 Glu Arg Asp Pro Ser Lys Ile Lys Trp Gly Asp Thr Gly Ala Glu Tyr  
 100 105 110  
 Val Val Glu Ser Thr Gly Val Phe Thr Thr Met Glu Lys Ala Gly  
 115 120 125

&lt;210&gt; 102

&lt;211&gt; 1225

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 102

atggcgggcgc ggctcgctcgtc ggggggtggcg gcggcagagg gggcgggcggc cctggcgggca 60  
 gcggagacgc cagccgtgac ggtggcagcg gcggcgcggg acctgggcct gggggaatga 120  
 ggcggccgcg gcgggccagc ggcggagccg tgtagcggag aagctcccc tccctgcttc 180  
 ccttggccga gccgggggcg cgcgcgcacg cgcccgcca gagcgggctc cccaccctc 240  
 gactcctgcg acccgcacgc cccccccacc cgggcccga ggatgatgaa gctcaagtcg 300  
 aaccagaccc gcacctacga cggcgacggc tacaagaagc gggccgcagc cctgtgtttc 360  
 cgcagcgaga gcgaggagga ggtgctactc gtgagcagta gtcgccatcc agacagatgg 420  
 attgtccctg gaggaggcat ggagcccag gaggagccaa gtgtggcagc agttcgtgaa 480  
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 tgggaagatt cagttaacat tggaaggaag agggaatggt ttaaaataga agacgccata 660  
 aaagtgtctg agtatcacia acccgtgcag gcatcatatt ttgaaacatt gaggcaaggc 720  
 tactcagcca acaatggcac cccagtcgtg gccaccacat actcggtttc tgctcagagc 780  
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 aggccaacag ccttcccctg ccttggatcc tgaagtgttc ctgtttgtct tatcctggcc 1140  
 ctggccagac gttttctttg atttttaatt tttttttttt attaaaagat accagtatga 1200  
 gaaaaaaaaa aaaaaaaaaa tcgag 1225

&lt;210&gt; 103

&lt;211&gt; 741

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 103

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agaaacctca atcggattca gcaaaggaat ggtgttatta tcactacata ccaaagtgtta 60
atcaataact ggcagcaact ttcaagcttt aggggccaaag agtttgtgtg ggactatgtc 120
atcctcgatg aagcacataa aataaaaacc tcactacta agtcagcaat atgtgctcgt 180
gctattcctg caagtaatcg cctcctcctc acaggaaccc caatccagaa taatttacia 240
gaactatggt ccctatttga ttttgcttgt caagggtccc tgctgggaac attaaaaact 300
tttaagatgg agtatgaaaa tcctattact agagcaagag agaaggatgc taccctcagga 360
gaaaaagcct tgggatttaa aatatctgaa aacttaatgg caatcataaa accctatttt 420
ctcaggagga ctaaagaaga cgtacagaag aaaaagtcaa gcaaccaga ggccagactt 480
aatgaaaaga atccagatgt tgatgccatt tgtgaaatgc cttccctttc caggagaaat 540
gatttaatta tttggatagc acttgtgcct ttacaagaag aaatatacag gaaatttgtg 600
tcttttagatc atatcaagga gttgctaag gagacgcgct cacccttggc tgagctaggt 660
gtcttaaaaga agctgtgtga tcactcctagg ctgctgtctg cacgggcttg ttgtttgcta 720
aatcttggga cattctctgc t 741

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&lt;210&gt; 104

&lt;211&gt; 321

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 104

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ttgctctgcg tcatcaaaga caccaaactg ctgtgctata aaagttccaa ggaccagcag 60
cctcagatgg aactgccact ccaaggctgt aacattacgt acatcccga agacagcaaa 120
aagaagaagc acgagctgaa gattactcag cagggcacgg acccgcttgt tctcgccgtc 180
cagagcaagg aacaggccga gcagtggtcg aaggatgatc aagaagccta cagtgggtgt 240
agtggccccc tggattcaga gtgtcctcct ccaccaagct ccccggtgca caaggcagaa 300
ctggagaaga aactgtcttc a 321

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&lt;210&gt; 105

&lt;211&gt; 389

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 105

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cagcactggc cacactataa aattcagggt cagaaaaaca gggtaagtca cagacagcaa 60
cgcttccagc atttattttc ttgacacca tgggcaattt gagaaaattt accttttagaa 120
cgaactctgt taaagggtaca gacagtacaa tactttttat tcagaagggt tctgcataaa 180
ggtgatagtc ttttgactta atatattatt gtctcctgcc ttgtgtttct ggaatgaatg 240
aagggtcatta tttagaagat aatctgggtt gtatttgtgt cgtcagattg aattttcatt 300
gcacatgcta cttaatgtct ttaccaata ataacaaagg gaaagaaaac caaatataga 360
tgtataataa ggaaaagctg gcctataga 389

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&lt;210&gt; 106

&lt;211&gt; 446

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 106

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gccacatttg ccttggatc agtttaaaaca ccaggctcctg tgtcacatct ttttgggtgcc 60
acaagtatca ctccattgtt cagagagtaa tgtattagtt ctgcccaatt cattcttcac 120
ttttatttct tccatttcat tagcatttat atcagctcaa gaagttaagg ttgaaaaatt 180
ttccacttca aattttcagt acagaaatgt gctgtgatgt ttgacaagac tatttcatag 240
taagttagtt aatgtttatt ggcctctgct ctctctgtg tcagacctag gaagcctgag 300
gattacttag ttgttctgtc tctgggtcca caggcagaat ttggcccatc caaagactgg 360
ccaagtgcc aaaaaaggcc tgattaggcc ctgaaattca gtgaaattct gcctgaagaa 420

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acctcttatt gaatttgaaa accata:

446

&lt;210&gt; 107

&lt;211&gt; 467

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 107

ccgccgctgc cgtcgccctc ctgggattgg agtctcgagc tttcttcggt cgttcgccgg 60  
cgggttcgcg cccttctcgc gcctcggggc tgcgaggctg gggagggggt tggagggggc 120  
tggtgatcgc cgcgtttaag ttgcgctcgg ggcggccatg tcggccggcg aggtcagcg 180  
cctagtgtcg gagctgagcg gcgggaccgg aggggatgag gaggaagagt ggctctatgg 240  
cgatgaagat gaagttgaaa ggccagaaga agaaaatgcc agtgctaact ctccatctgg 300  
aattgaagat gaaactgctg aaaatgggtg accaaaaaccg aaagtgactg agaccgaaga 360  
tgatagtgat agtgacagcg atgatgatga agatgatgtg catgtcacta taggagacat 420  
taaaacggga gcaccacagt atgggagtta tggtagaca cctgtaa 467

&lt;210&gt; 108

&lt;211&gt; 491

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 108

gaaagataca acttcccaa cccaaaccg tttgtggagg acgacatgga taagaatgaa 60  
atgcgctctg ttgcgtaccg ttaccgcagg tggagcttg gagatgatat tgaccttatt 120  
gtcgttgtg agcacgatgg cgtcatgact ggagccaacg gggaggtgct ctccatcaac 180  
atcaagacac tcaatgagtg ggattccagg cactgtaatg gcgttgactg gcgtcagaag 240  
ctggactctc agcgaggggc tgcattgcc acggagctga agaacaacag ctacaagttg 300  
gcccgggtga cctgctgtgc tttgtgggt ggatctgagt acctcaagct tggttatgtg 360  
tctcggtacc acgtgaaaga ctctcacgc cacgtcatcc taggcacca gcagttcaag 420  
cctaattgagt ttgccagcca gatcaacctg agcgtggaga atgcctgagg cattttacgc 480  
tgcgtcattg a 491

&lt;210&gt; 109

&lt;211&gt; 489

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 109

ctcagatagt actgaaccct ttatcaacta tgttttttca gtctgacaac caaggcggct 60  
actaagtgac taaggggcag gtagtataca gtgtggataa gcaggacaaa ggggtgattc 120  
acatcccagg caggacagag caggagatca tgagatttca tcaactcagga tggcttgtga 180  
tttattttat tttattcttt ttttttttgg agatggagtc tcaactcttc ccaggctgga 240  
gtgcagtggt gcgatcttgg ctactgcaa cctctgcctc ctgggttcaa gcagttctcc 300  
tgctcagcc tcccaagtag ctgggattac aggcgtccgc caccatgccc agccaatttt 360  
tgtactttta gtagagatgg ggtttacca tgttggccag gctggtctcg aactcctgac 420  
ctcaggtgat ccactcgct cggcctccca aagtgtggg attataggca tgcgccacca 480  
tgcccgggc 489

&lt;210&gt; 110

&lt;211&gt; 391

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 110

gcggagtcg ctggctgacc cgagcgctgg tctccgccgg gaaccctggg gcatggagag 60  
 gtctgagtac ctcgcccgcg gcgcacgctg catcgcgag ccaggctgcc gctgtcccag 120  
 tggagttcca ggagcaccac ctgagtgagg tgcagaatat ggcattctgag gagaagctgg 180  
 agcaggtgct gagttccatg aaggagaaca aagtggccat cattggaaag attcataccc 240  
 cgatggagta taagggggag ctagcctcct atgatatgcg gctgaggcgt aagttggact 300  
 tatttgccaa cgtaatccat gtgaagtcac ttcctgggta tatgactcgg cacaacaatc 360  
 tagacctggt gatcattcga gacgagacag a 391

<210> 111

<211> 172

<212> PRT

<213> Homo sapiens

<400> 111

Met Met Lys Leu Lys Ser Asn Gln Thr Arg Thr Tyr Asp Gly Asp Gly  
 1 5 10 15

Tyr Lys Lys Arg Ala Ala Cys Leu Cys Phe Arg Ser Glu Ser Glu Glu  
 20 25 30

Glu Val Leu Leu Val Ser Ser Ser Arg His Pro Asp Arg Trp Ile Val  
 35 40 45

Pro Gly Gly Gly Met Glu Pro Glu Glu Glu Pro Ser Val Ala Ala Val  
 50 55 60

Arg Glu Val Cys Glu Glu Ala Gly Val Lys Gly Thr Leu Gly Arg Leu  
 65 70 75 80

Val Gly Ile Phe Glu Asn Gln Glu Arg Lys His Arg Thr Tyr Val Tyr  
 85 90 95

Val Leu Ile Val Thr Glu Val Leu Glu Asp Trp Glu Asp Ser Val Asn  
 100 105 110

Ile Gly Arg Lys Arg Glu Trp Phe Lys Ile Glu Asp Ala Ile Lys Val  
 115 120 125

Leu Gln Tyr His Lys Pro Val Gln Ala Ser Tyr Phe Glu Thr Leu Arg  
 130 135 140

Gln Gly Tyr Ser Ala Asn Asn Gly Thr Pro Val Val Ala Thr Thr Tyr  
 145 150 155 160

Ser Val Ser Ala Gln Ser Ser Met Ser Gly Ile Arg  
 165 170

<210> 112

<211> 247

<212> PRT

<213> Homo sapiens

<400> 112

Arg Asn Leu Asn Arg Ile Gln Gln Arg Asn Gly Val Ile Ile Thr Thr

1                      5                      10                      15  
 Tyr Gln Met Leu Ile Asn Asn Trp Gln Gln Leu Ser Ser Phe Arg Gly  
                                  20                      25                      30  
 Gln Glu Phe Val Trp Asp Tyr Val Ile Leu Asp Glu Ala His Lys Ile  
                                  35                      40                      45  
 Lys Thr Ser Ser Thr Lys Ser Ala Ile Cys Ala Arg Ala Ile Pro Ala  
                                  50                      55                      60  
 Ser Asn Arg Leu Leu Leu Thr Gly Thr Pro Ile Gln Asn Asn Leu Gln  
                                  65                      70                      75                      80  
 Glu Leu Trp Ser Leu Phe Asp Phe Ala Cys Gln Gly Ser Leu Leu Gly  
                                  85                      90                      95  
 Thr Leu Lys Thr Phe Lys Met Glu Tyr Glu Asn Pro Ile Thr Arg Ala  
                                  100                      105                      110  
 Arg Glu Lys Asp Ala Thr Pro Gly Glu Lys Ala Leu Gly Phe Lys Ile  
                                  115                      120                      125  
 Ser Glu Asn Leu Met Ala Ile Ile Lys Pro Tyr Phe Leu Arg Arg Thr  
                                  130                      135                      140  
 Lys Glu Asp Val Gln Lys Lys Lys Ser Ser Asn Pro Glu Ala Arg Leu  
                                  145                      150                      155                      160  
 Asn Glu Lys Asn Pro Asp Val Asp Ala Ile Cys Glu Met Pro Ser Leu  
                                  165                      170                      175  
 Ser Arg Arg Asn Asp Leu Ile Ile Trp Ile Arg Leu Val Pro Leu Gln  
                                  180                      185                      190  
 Glu Glu Ile Tyr Arg Lys Phe Val Ser Leu Asp His Ile Lys Glu Leu  
                                  195                      200                      205  
 Leu Met Glu Thr Arg Ser Pro Leu Ala Glu Leu Gly Val Leu Lys Lys  
                                  210                      215                      220  
 Leu Cys Asp His Pro Arg Leu Leu Ser Ala Arg Ala Cys Cys Leu Leu  
                                  225                      230                      235                      240  
 Asn Leu Gly Thr Phe Ser Ala  
                                  245

&lt;210&gt; 113

&lt;211&gt; 107

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 113

Leu Leu Cys Val Ile Lys Asp Thr Lys Leu Leu Cys Tyr Lys Ser Ser

<210> 114  
<211> 155  
<212> PRT  
<213> Homo sapiens

<400> 114																	
Glu	Arg	Tyr	Asn	Phe	Pro	Asn	Pro	Asn	Pro	Phe	Val	Glu	Asp	Asp	Met		
1				5					10					15			
Asp	Lys	Asn	Glu	Ile	Ala	Ser	Val	Ala	Tyr	Arg	Tyr	Arg	Arg	Trp	Lys		
			20					25					30				
Leu	Gly	Asp	Asp	Ile	Asp	Leu	Ile	Val	Arg	Cys	Glu	His	Asp	Gly	Val		
		35					40					45					
Met	Thr	Gly	Ala	Asn	Gly	Glu	Val	Ser	Phe	Ile	Asn	Ile	Lys	Thr	Leu		
	50					55					60						
Asn	Glu	Trp	Asp	Ser	Arg	His	Cys	Asn	Gly	Val	Asp	Trp	Arg	Gln	Lys		
65					70					75					80		
Leu	Asp	Ser	Gln	Arg	Gly	Ala	Val	Ile	Ala	Thr	Glu	Leu	Lys	Asn	Asn		
				85					90					95			
Ser	Tyr	Lys	Leu	Ala	Arg	Trp	Thr	Cys	Cys	Ala	Leu	Leu	Ala	Gly	Ser		
			100					105					110				
Glu	Tyr	Leu	Lys	Leu	Gly	Tyr	Val	Ser	Arg	Tyr	His	Val	Lys	Asp	Ser		
	115						120					125					
Ser	Arg	His	Val	Ile	Leu	Gly	Thr	Gln	Gln	Phe	Lys	Pro	Asn	Glu	Phe		
	130					135					140						
Ala	Ser	Gln	Ile	Asn	Leu	Ser	Val	Glu	Asn	Ala							



145

150

155

<210> 115  
 <211> 129  
 <212> PRT  
 <213> Homo sapiens

&lt;400&gt; 115

Gly Val Arg Trp Leu Thr Arg Ala Leu Val Ser Ala Gly Asn Pro Gly  
 1 5 10 15

Ala Trp Arg Gly Leu Ser Thr Ser Ala Ala Ala His Ala Ala Ser Arg  
 20 25 30

Ser Gln Ala Ala Val Pro Val Glu Phe Gln Glu His His Leu Ser  
 35 40 45

Glu Val Gln Asn Met Ala Ser Glu Glu Lys Leu Glu Gln Val Leu Ser  
 50 55 60

Ser Met Lys Glu Asn Lys Val Ala Ile Ile Gly Lys Ile His Thr Pro  
 65 70 75 80

Met Glu Tyr Lys Gly Glu Leu Ala Ser Tyr Asp Met Arg Leu Arg Arg  
 85 90 95

Lys Leu Asp Leu Phe Ala Asn Val Ile His Val Lys Ser Leu Pro Gly  
 100 105 110

Tyr Met Thr Arg His Asn Asn Leu Asp Leu Val Ile Ile Arg Glu Gln  
 115 120 125

Thr

<210> 116  
 <211> 550  
 <212> DNA  
 <213> Homo sapiens

&lt;400&gt; 116

gaattcggca ccagcctcag agccccccag cccggctacc accccctgcg gaaaggtacc 60  
 catctgcatt cctgcccgtc gggacctggt ggacagtcca gcctccttgg cctctagcct 120  
 tggctcaccg ctgcctagag ccaaggagct catcctgaat gaccttcccg ccagcactcc 180  
 tgcctccaaa tcctgtgact cctccccgcc ccaggacgct tccacccccca ggcccagctc 240  
 ggccagtcac ctctgccagc ttgctgcca gccagcacct tccacggaca gcgtcgccct 300  
 gaggagcccc ctgactctgt ccagtccctt caccacgtcc ttcagcctgg gctcccacag 360  
 cactctcaac ggagacctct ccgtgcccag ctctacgtc agcctccacc tgtcccccca 420  
 ggtcagcagc tctgtggtgt acggacgtc ccccgtagtgc gcatttgagt ctcatcccca 480  
 tctccgaggg tcatccgtct cttcctccct acccagcatc cctgggggaa agccggccta 540  
 ctccctccac 550

<210> 117  
 <211> 154

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 117

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ttctgagggg aagccgagtg gagtgggcca cccggcggcg gtgacaatga gttttcttgg 60
aggctttttt ggtccatttt gtgagattga tgttgccctt aatgatgggg aaaccaggaa 120
aatggcagaa atgaaaactg aggatggcaa agta 154

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&lt;210&gt; 118

&lt;211&gt; 449

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 118

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gaattcggca ccagggcccg cagcccgagt gtcgcgcgcca tggcttcgcc gcagctctgc 60
cgcgcgctgg tgcggcgcca atgggtggcg gaggcgctgc gggccccgcg cgctgggcag 120
cctctgcagc tgctggacgc ctcttggtac ctgcggaagc tggggcgcca cgcgcgacgc 180
gagttcgagg agcgccacat cccggcgccc gttttcttcg acatcgacca gtgcagcgac 240
cgcacctcgc cctacgacca catgctgccc gggggcgagc atttcgcgga gtacgcaggc 300
cgcttgggcy tggggcgggc caccacgctc gtgatctacg acgcccagca ccagggcctc 360
tactccgccc cgcgcgctctg gtggatgttc cgcgccctcg gccaccacgc cgtgtcactg 420
cttgatggcg gcctccgcca ctggctgcg 449

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&lt;210&gt; 119

&lt;211&gt; 642

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 119

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gaattcggca cgagcagtaa cccgaccgcc gctggtcttc gctggacacc atgaatcaca 60
atgtccaaac cttcttctct cctgtcaaca gtggccagcc ccccaactat gagatgctca 120
aggaggagca cgaggtggct gtgctggggg cgccccacaa cctgctccc ccgacgtcca 180
ccgtgatcca catccgcagc gagacctccg tgccccacca tgcgtctgg tccctgttca 240
acacctctt catgaacccc tgctgectgg gttcatagc attcgctac tccgtgaagt 300
ctagggacag gaagatggtt ggcgacgtga ccggggccca ggccatgcc tccaccgcca 360
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tcccagtgt gatcttccag gcctatggat agatcaggag gcatcactga ggccaggagc 480
tctgcccatt acctgtatcc caggtactcc aacttccatt cctcgccctg cccccggagc 540
cgagtccctgt atcagccctt tatcctcaca cgcttttcta caatggcatt caataaagtg 600
cacgtgtttc tggtgaaaaa aaaaaaaaaa aaaaaactcg ag 642

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&lt;210&gt; 120

&lt;211&gt; 603

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 120

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gaattcggca cgagccacaa cagccactac gactgcatcc actggatcca cggccacccc 60
gtcctccacc ccgggaacag cccccctcc caaagtgtg accagcccgg ccaccacacc 120
catgtccacc atgtccacaa tccacacctc ctctactcca gagaccacc acacctccac 180
agtgtgacc accacagcca ccatgacaag ggccaccaat tccacggcca cacctctctc 240
cactctgggg acgaccggga tctcactga gctgaccaca acagccacta caactgcagc 300
cactggatcc acggccaccc tgtcctccac cccagggacc acctggatcc tcacagagcc 360
gagcactata gccaccgtga tgggtcccac cggttccacg gccaccgct cctccactct 420
gggaacagct cacaccccca aagtgggtgac caccatggcc actatgccc cagccactgc 480

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ctccacggtt cccagctcgt ccaccgtggg gaccaccgc acccctgcag tgctccccag 540  
 cagcctgccca accttcagcg tgtccactgt gtcctcctca gtcctcacca ccctgagacc 600  
 cac 603

<210> 121  
 <211> 178  
 <212> PRT  
 <213> Homo sapiens

<400> 121

Ser Glu Pro Pro Ser Pro Ala Thr Thr Pro Cys Gly Lys Val Pro Ile  
 1 5 10 15

Cys Ile Pro Ala Arg Arg Asp Leu Val Asp Ser Pro Ala Ser Leu Ala  
 20 25 30

Ser Ser Leu Gly Ser Pro Leu Pro Arg Ala Lys Glu Leu Ile Leu Asn  
 35 40 45

Asp Leu Pro Ala Ser Thr Pro Ala Ser Lys Ser Cys Asp Ser Ser Pro  
 50 55 60

Pro Gln Asp Ala Ser Thr Pro Arg Pro Ser Ser Ala Ser His Leu Cys  
 65 70 75 80

Gln Leu Ala Ala Lys Pro Ala Pro Ser Thr Asp Ser Val Ala Leu Arg  
 85 90 95

Ser Pro Leu Thr Leu Ser Ser Pro Phe Thr Thr Ser Phe Ser Leu Gly  
 100 105 110

Ser His Ser Thr Leu Asn Gly Asp Leu Ser Val Pro Ser Ser Tyr Val  
 115 120 125

Ser Leu His Leu Ser Pro Gln Val Ser Ser Ser Val Val Tyr Gly Arg  
 130 135 140

Ser Pro Val Met Ala Phe Glu Ser His Pro His Leu Arg Gly Ser Ser  
 145 150 155 160

Val Ser Ser Ser Leu Pro Ser Ile Pro Gly Gly Lys Pro Ala Tyr Ser  
 165 170 175

Phe His

<210> 122  
 <211> 36  
 <212> PRT  
 <213> Homo sapiens

<400> 122

Met Ser Phe Leu Gly Gly Phe Phe Gly Pro Ile Cys Glu Ile Asp Val  
 1 5 10 15

Ala Leu Asn Asp Gly Glu Thr Arg Lys Met Ala Glu Met Lys Thr Glu  
 20 25 30

Asp Gly Lys Val  
 35

<210> 123

<211> 136

<212> PRT

<213> Homo sapiens

<400> 123

Met Ala Ser Pro Gln Leu Cys Arg Ala Leu Val Ser Ala Gln Trp Val  
 1 5 10 15

Ala Glu Ala Leu Arg Ala Pro Arg Ala Gly Gln Pro Leu Gln Leu Leu  
 20 25 30

Asp Ala Ser Trp Tyr Leu Pro Lys Leu Gly Arg Asp Ala Arg Arg Glu  
 35 40 45

Phe Glu Glu Arg His Ile Pro Gly Ala Ala Phe Phe Asp Ile Asp Gln  
 50 55 60

Cys Ser Asp Arg Thr Ser Pro Tyr Asp His Met Leu Pro Gly Ala Glu  
 65 70 75 80

His Phe Ala Glu Tyr Ala Gly Arg Leu Gly Val Gly Ala Ala Thr His  
 85 90 95

Val Val Ile Tyr Asp Ala Ser Asp Gln Gly Leu Tyr Ser Ala Pro Arg  
 100 105 110

Val Trp Trp Met Phe Arg Ala Phe Gly His His Ala Val Ser Leu Leu  
 115 120 125

Asp Gly Gly Leu Arg His Trp Leu  
 130 135

<210> 124

<211> 133

<212> PRT

<213> Homo sapiens

<400> 124

Met Asn His Thr Val Gln Thr Phe Phe Ser Pro Val Asn Ser Gly Gln  
 1 5 10 15

Pro Pro Asn Tyr Glu Met Leu Lys Glu Glu His Glu Val Ala Val Leu  
 20 25 30

Gly Ala Pro His Asn Pro Ala Pro Pro Thr Ser Thr Val Ile His Ile  
 35 40 45

Arg Ser Glu Thr Ser Val Pro Asp His Val Val Trp Ser Leu Phe Asn  
50 55 60

Thr Leu Phe Met Asn Pro Cys Cys Leu Gly Phe Ile Ala Phe Ala Tyr  
65 70 75 80

Ser Val Lys Ser Arg Asp Arg Lys Met Val Gly Asp Val Thr Gly Ala  
85 90 95

Gln Ala Tyr Ala Ser Thr Ala Lys Cys Leu Asn Ile Trp Ala Leu Ile  
100 105 110

Leu Gly Ile Leu Met Thr Ile Leu Leu Ile Val Ile Pro Val Leu Ile  
115 120 125

Phe Gln Ala Tyr Gly  
130

<210> 125

<211> 195

<212> PRT

<213> Homo sapiens

<400> 125

Thr Thr Ala Thr Thr Thr Ala Ser Thr Gly Ser Thr Ala Thr Pro Ser  
1 5 10 15

Ser Thr Pro Gly Thr Ala Pro Pro Pro Lys Val Leu Thr Ser Pro Ala  
20 25 30

Thr Thr Pro Met Ser Thr Met Ser Thr Ile His Thr Ser Ser Thr Pro  
35 40 45

Glu Thr Thr His Thr Ser Thr Val Leu Thr Thr Thr Ala Thr Met Thr  
50 55 60

Arg Ala Thr Asn Ser Thr Ala Thr Pro Ser Ser Thr Leu Gly Thr Thr  
65 70 75 80

Arg Ile Leu Thr Glu Leu Thr Thr Thr Ala Thr Thr Thr Ala Ala Thr  
85 90 95

Gly Ser Thr Ala Thr Leu Ser Ser Thr Pro Gly Thr Thr Trp Ile Leu  
100 105 110

Thr Glu Pro Ser Thr Ile Ala Thr Val Met Val Pro Thr Gly Ser Thr  
115 120 125

Ala Thr Ala Ser Ser Thr Leu Gly Thr Ala His Thr Pro Lys Val Val  
130 135 140

Thr Thr Met Ala Thr Met Pro Thr Ala Thr Ala Ser Thr Val Pro Ser  
145 150 155 160

Ser Ser Thr Val Gly Thr Thr Arg Thr Pro Ala Val Leu Pro Ser Ser  
 165 170 175

Leu Pro Thr Phe Ser Val Ser Thr Val Ser Ser Ser Val Leu Thr Thr  
 180 185 190

Leu Arg Pro  
 195

<210> 126  
 <211> 509  
 <212> DNA  
 <213> homo sapien

<400> 126  
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 atccctcgtg gccataaagg gcaaccaaga gagcccaaaa gccactggag tctttaccac 120  
 actgcagcct gggagctcta ttccacctta caacaccgag gtgactgaga ccaccattgt 180  
 gatcacatgg acgcctgctc caagaattgg ttttaagctg ggtgtacgac caagccaggg 240  
 aggagaggca ccacgagaag tgacttcaga ctcaggaagc atcgttgtgt ccggccttgac 300  
 tccaggagta gaatacgtct acaccatcca agtcctgaga gatggacagg aaagagatgc 360  
 gccaatgtta aacaaagtgg tgacaccatt gtctccacca acaaaattgc atctggaggc 420  
 aaaccctgac actggagtgc tcacagtctc ctggagagga gcaccacccc agacattact 480  
 gggatatagaa ttaccacaac ccctacaaa 509

<210> 127  
 <211> 500  
 <212> DNA  
 <213> homo sapien

<400> 127  
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 ttgctgagag gacgcgtcta gtctgaagg ccaagggaaat caggcatgaa gtcaccaata 180  
 tcaacctgaa aaataagcct gagtggttct ttaagaaaaa tccctttggt ctgggtgccag 240  
 ttctggaaaa cagtcagggt cagctgatct acgagtctgc catcacctgt gagtacctgg 300  
 atgaagcata cccagggaag aagctgttgc cggatgaccc ctatgagaaa gcttgccaga 360  
 agatgatctt agagttgttt tctaagggtc catccttggg aggaagcttt attagaagcc 420  
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<210> 128  
 <211> 500  
 <212> DNA  
 <213> homo sapien

<400> 128  
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 tgaatgcaga agcttgctgg ccaaaagatg tgggaattgt tgcccttgag atctattttc 180  
 cttctcaata tgttgatcaa gcagagttgg aaaaatatga tgggttagat gctggaaagt 240  
 ataccattgg cttggggccag gccaaagatg gcttctgcac agatagagaa gatattaact 300  
 ctctttgcat gactgtggtt cagaatctta tggagagaaa taacctttcc tatgattgca 360

ttgggaggct ggaagttgga acagagacaa tcatcgacaa atcaaagtct gtgaagacta 420  
 atttgatgca gctgtttgaa gagtctggga atacagatat agaaggaatc gacacaacta 480  
 atgcatgcta tggaggcaca 500

<210> 129  
 <211> 497  
 <212> DNA  
 <213> homo sapien

<400> 129  
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 cactgtagt ggtgttgac aagttggtat ggcgtgtgct atcagcattc tgggaaagtc 180  
 tctggctgat gaacttgctc ttgtggatgt tttggaagat aagcttaaag gagaaatgat 240  
 ggatctgcag catgggagct tatttcttca gacacctaaa attgtggcag ataaagatta 300  
 ttctgtgacc gccaatctta agattgtagt ggtaactgca ggagtcgctc agcaagaagg 360  
 ggagagtcgg ctcaatctgg tgcagagaaa tgttaatgtc ttcaaattca ttattcctca 420  
 gatcgtcaag tacagtcctg attgcatcat aattgtgggt tccaaccagc tggacattct 480  
 tacgtatgtt acctgga 497

<210> 130  
 <211> 383  
 <212> DNA  
 <213> homo sapien

<400> 130  
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 tccgcaccgc cccgcgccgc cgctgctttg cgcgctgtcc ctggcgctgt gcgcgctgtc 120  
 gctgcccgct cgcgcggcca ctgcgtcgcg gggggcgctc caggcggggg cgccccaggg 180  
 gcgggtgccc gaggcgcggc ccaacagcat ggtggtggaa caccacagat tctcaaggc 240  
 agggaaaggag cctggcctgc agatctggcg tgtggagaaa gtctgatctg gtggcccggt 300  
 cccaccaacc tttatggaga cttcttcacg ggcgacgctt acgtcatcct gaagacagtg 360  
 cagcttaaga acggaaaatc ttg 383

<210> 131  
 <211> 509  
 <212> DNA  
 <213> homo sapien

<400> 131  
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 agacaccatg gggaaggtga aggtcggagt caacggattt ggtcgtattg ggcgcctggt 120  
 caccagggct gcttttaact ctggtaaaagt ggatattgtt gccatcaatg accccttcat 180  
 tgacctcaac tacatggttt acatgttcca atatgattcc accatggca aattccatgg 240  
 caccgtcaag gctgagaacg ggaagcttgt catcaatgga aatcccatca ccatcttcca 300  
 ggagcgagat ccctccaaa tcaagtgggg cgatgctggc gctgagtacg tcgtggagtc 360  
 cactggccgt cttcaccacc atggagaagg ctggggctca tttgcagggg ggagccaaaa 420  
 gggcatcat ctctgcccc tctgctgacg ccccatgtt cgtcatgggt gtgaaccatg 480  
 agaagtatga caacagcctc aagatcatc 509

<210> 132  
 <211> 357  
 <212> DNA  
 <213> homo sapien

&lt;400&gt; 132

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ggaggatcct	cttcttggtg	gcagcagcaa	caggtgcca	ctcccaggtg	caactggtgc	120
aatctgggtc	tgagttgaag	aagcctgggg	cctcagtga	ggtttcctgc	aaggcttctg	180
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&lt;210&gt; 133

&lt;211&gt; 468

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 133

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&lt;210&gt; 134

&lt;211&gt; 214

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 134

gaattcggca	cgagctgctg	cctgctgagc	tctgttctct	ccagcacctc	ccaaccact	60
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cccgcaccag	cttcacctcc	gtgtcccgg	ccgg			214

&lt;210&gt; 135

&lt;211&gt; 355

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 135

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&lt;210&gt; 136

&lt;211&gt; 242

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 136

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 <213> homo sapien

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caatgatcgc ttggcgggtct acatcgaccg tgtgcgctcg ctggaaacgg agaacgcagg	360
gctgcgcctt cgcatcaccg agtctgaaga ggtggtcagc cgcgagggtg ccggcatcaa	420
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 <211> 448  
 <212> DNA  
 <213> homo sapien

<400> 138	
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 <212> DNA  
 <213> homo sapien

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<210> 140  
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 <212> DNA  
 <213> homo sapien

&lt;400&gt; 140

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&lt;210&gt; 141

&lt;211&gt; 483

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 141

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tga						483

&lt;210&gt; 142

&lt;211&gt; 500

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 142

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gtttgggtggc	cgggggccgag	gtgggatccc	gggcacaggc	agaagccagc	cagagaagaa	480
gcctggcaga	caggcgggca					500

&lt;210&gt; 143

&lt;211&gt; 400

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 143

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&lt;210&gt; 144

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 ctg 243

<210> 145  
 <211> 450  
 <212> DNA  
 <213> homo sapien

<400> 145  
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<210> 146  
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 <212> DNA  
 <213> homo sapien

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<210> 147  
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 <211> 503  
 <212> DNA  
 <213> Homo sapien

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 <211> 781  
 <212> DNA  
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<210> 151

<211> 3275

<212> DNA

<213> Homo sapien

<400> 151

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&lt;211&gt; 2179

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 152

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<211> 2109

<212> DNA

<213> Homo sapien

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<211> 1411

<212> DNA

<213> homo sapien

<400> 154

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&lt;211&gt; 678

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 155

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&lt;212&gt; DNA

&lt;213&gt; Homo sapien

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&lt;211&gt; 2313

&lt;212&gt; DNA

&lt;213&gt; homo sapien

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&lt;211&gt; 2114

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 158

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&lt;210&gt; 159

&lt;211&gt; 278

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 159

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&lt;210&gt; 160

&lt;211&gt; 848

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 160

gaattcggca	cgagccccag	aggagctcgg	cctgcgctgc	gccacgatgt	ccggggagtc	60
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aactcgag						848

&lt;210&gt; 161

&lt;211&gt; 432

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 161

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ggaaggggaag	ggcccaagta	aagcacagcg	cgggagccta	gagcacatga	agctgatcct	180
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cctcctgtcc	cagcgagagc	aggaatatgt	ggtcctgcag	cagcaactgc	aggaagccag	360
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cctagcccag	ag					432

&lt;210&gt; 162

&lt;211&gt; 433

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 162

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ttcctgactc	gag					433

&lt;210&gt; 163

&lt;211&gt; 432

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 163

gaattcggca	ccagatgagg	ccaacgaggt	gacggacagc	gcgtacatgg	gctccgagag	60
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ccatggccag	tctgtcatca	cggatgctcg	ggggcaggag	cactttgagg	actacggtga	300
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cctgcaccag	tc					432

&lt;210&gt; 164

&lt;211&gt; 395

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 164

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<210> 165  
 <211> 503  
 <212> DNA  
 <213> homo sapien

<400> 165

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gagaaaggag	aggtaaaaat	gtgtacatc	agctctcagt	aaccctagaa	gacttatata	480
atggtgcaac	aagaaaactg	gct				503

<210> 166  
 <211> 893  
 <212> DNA  
 <213> homo sapien

<400> 166

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acaataaatt	tttttggtc	aaatttaaaa	aaaaaaaaaa	aaaaaaactc	gag	893

<210> 167  
 <211> 549  
 <212> DNA  
 <213> homo sapien

<400> 167

gaattcggca	cgagcccaga	tcccaggtc	cgacagcgcc	cgcccagat	ccccacgcct	60
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gcgcgcccgc	ctgcagctgg	agctgagcaa	agtgcgtgaa	gagtttaagg	agctgaaagc	540
gcgcaatac						549

<210> 168  
 <211> 547  
 <212> DNA  
 <213> homo sapien

<400> 168

gaattcggca	cgagatggcg	gcaggggtcg	aagcggcggc	ggaggtggcg	gcgacggaga	60
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gtctgagcgg	aagaccactg	aaagtcaaag	aagatcctga	tggtgaacat	gccaggagag	480
caatgcaaaa	ggctggaaga	cttgaagca	cagtatttgt	agcaaactcg	gattataaag	540
ttggctg						547

<210> 169  
 <211> 547  
 <212> DNA  
 <213> homo sapien

<400> 169

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aaacctc						547

<210> 170  
 <211> 838  
 <212> DNA  
 <213> homo sapien

<400> 170

gaattcggca	ccagaggagc	tcggcctgcg	ctgcgccacg	atgtccgggg	agtcagccag	60
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cagcatgagg	ttctgcccgt	ttgctgagag	gacgcgtcta	gtcctgaagg	ccaagggaa	180
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agcaataaag	ctatgtctga	tattttcctt	cactaaaaaa	aaaaaaaaaa	aactcgag	838

<210> 171  
 <211> 547  
 <212> DNA  
 <213> homo sapien

<400> 171

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catcgagaac gtcaaagcaa agatccagga caaggaaggc attcctctg accagcagag	420
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gaccctg	547

<210> 172  
 <211> 608  
 <212> DNA  
 <213> homo sapien

<400> 172

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ggaccacagg ctgccatag ggggccagt cggccctgt ccctgtcctg aaggccctgg	360
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ccactgccgg gcaggctata cggggctgcg atgtgaagct tgtgccctg ggcactttgg	480
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aatggatcct gatgcctgtg acccccacac ggggcaatgc ctgcgtgtt tacaccacac	600
agagggtc	608

<210> 173  
 <211> 543  
 <212> DNA  
 <213> homo sapien

<400> 173

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acc	543

<210> 174  
 <211> 548  
 <212> DNA

&lt;213&gt; homo sapien

&lt;400&gt; 174

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ccctaagggt gaaggagaac gacctgctca gaatgagaag aggaaggaga aaaacataaa	180
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aatgatta	548

&lt;210&gt; 175

&lt;211&gt; 604

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 175

gaattcggca ccagaggacc tccaggacat gtccatcgtc cataccatcg aggagattga	60
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gcagtccaac gagcacctgc gccgccagtt cgccagccag gccaatgttg tggggccctg	360
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ggaccagctg agccacctga agcagtatga acgcagcatc gtggactaca agcccaacct	480
ggacctgctg gagcagcagc accagcttat ccaggaggcc ctcatcttcg acaacaagca	540
caccaactat accatggagc acatccgcgt gggctgggag cagctgctca ccaccattgc	600
ccgg	604

&lt;210&gt; 176

&lt;211&gt; 486

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 176

gaattcggca ccagccaagc tcactattga atccacgccg ttcaatgtcg cagaggggaa	60
ggaggttctt ctactgccc acaacctgcc ccagaatcgt attggttaca gctggtacaa	120
aggcgaaga gtggatggca acagtctaata ttaggatata gtaataggaa ctcaacaagc	180
tacccaggg ccgcataca gtggtcgaga gacaatata cccaatgcat ccctgctgat	240
ccagaacgtc acccagaatg acacaggatt ctatacccta caagtcataa agtcagatct	300
tgtgaatgaa gaagcaaccg gacagttcca tgtatacccg gagctgccc agccctccat	360
ctccagcaac aactccaacc ccgtggagga caaggatgct gtggccttca cctgtgaacc	420
tgaggttcag aacacaacct acctgtggtg ggtaaatggt cagagcctcc cggtcagtc	480
caaggc	486

&lt;210&gt; 177

&lt;211&gt; 387

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 177

gaattcggca ccagggacag cagaccagac agtcacagca gccttgacaa aacgttctctg	60
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gaactcaagc tcttctccac agaggaggac agagcagaca gcagagacca tggagctctcc	120
ctcgcccccct cccacacagat ggtgcatccc ctggcagagg ctctgctca cagcctcact	180
tctaaccttc tggaaaccgc ccaccactgc caagctcact attgaatcca cgccgttcaa	240
tgctgcagag gggaaggagg tgcttctact tgtccacaat ctgccccagc atctttttgg	300
ctacagctgg tacaaagggtg aaagagtggg tggcaaccgt caaattatag gatatgtaat	360
aggaactcaa caagctaccc cagggcc	387

&lt;210&gt; 178

&lt;211&gt; 440

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 178

gaattcggca cgaggagaag cagaaaaaca aggaatttag ccagacttta gaaaatgaga	60
aaaatacctt actgagtcag atatcaacaa aggatgggtga actaaaaatg cttcaggagg	120
aagtaaccaa aatgaacctg ttaaatacagc aaatccaaga agaactctct agagttacca	180
aactaaagga gacagcagaa gaagagaaag atgatttggg agagaggctt atgaatcaat	240
tagcagaact taatggaagc attgggaatt actgtcagga tgttacagat gcccaaataa	300
aaaatgagct attggaatct gaaatgaaga accttaaaaa gtgtgtgagt gaattggaag	360
aagaaaagca gcagttagtc aaggaaaaaa ctaagggtgga atcagaaata cgaaaggaat	420
atttgagaaa aatacaaggt	440

&lt;210&gt; 179

&lt;211&gt; 443

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 179

gaattcggca ccagcggggg gctacggcgg cggctacggc ggcgtcctga ccgcgtccga	60
cgggctgctg gcgggcaacg agaagctaac catgcagaac ctcaacgacc gcctggcctc	120
ctacctggac aaggtgcgcg ccctggaggc ggccaacggc gagctagagg tgaagatccg	180
cgactggtag cagaagcagg ggcctggggee eteegcgac tacagccact actacacgac	240
catccaggac ctgcgggaca agattcttgg tgccaccatt gagaactcca ggattgtcct	300
gcagatcgac aacgcccgtc tggctgcaga tgacttccga accaagtttg agacggaaca	360
ggctctgcgc atgagcgtgg aggccgacat caacggcctg cgcagggtgc tggatgagct	420
gaccctggcc aggaccgacc tgg	443

&lt;210&gt; 180

&lt;211&gt; 403

&lt;212&gt; DNA

&lt;213&gt; homo sapien

&lt;400&gt; 180

gaattcggca cgaggttatg agagtcgact tcaatgttcc tatgaagaac aaccagataa	60
caaacaacca gaggattaag gctgctgtcc caagcatcaa attctgcttg gacaatggag	120
ccaagtcggt agtccttatg agccacctag gccggcctga tgggtgtgcc atgcctgaca	180
agtactcctt agagccagtt gctgtagaac tcagatctct gctgggcaag gatgttctgt	240
tcttgaagga ctgtgtaggc ccagaagtgg agaaagcctg tgccaaccca gctgctgggt	300
ctgtcatcct gctggagaac ctccgctttc atgtggagga agaagggaag ggaaaagatg	360
cttctgggaa caaggttaaa gccgagccag ccaaaataga agc	403

&lt;210&gt; 181

&lt;211&gt; 493

&lt;212&gt; DNA

&lt;213&gt; homo sapien

<400> 181  
 gaattcggca ccagcagagg tctccagagc cttctctctc ctgtgcaaaa tggcaactct 60  
 taaggaaaaa ctcattgcac cagttgcgga agaagaggca acagttccaa acaataagat 120  
 cactgtagtg ggtgttggac aagttggtat ggcgtgtgct atcagcattc tgggaaagtc 180  
 tetggctgat gaacttgctc ttgtggatgt tttggaagat aagcttaaag gagaaatgat 240  
 ggatctgcag catgggagct tatttcttca gacacctaaa attgtggcag ataaagatta 300  
 ttctgtgacc gccaatctca agattgtagt ggtaactgca ggagtccgct agcaagaagg 360  
 ggagagtcgg ctcaatctgg tgcagagaaa tgtaaatgtc ttcaaattca ttattcctca 420  
 gatcgtcaag tacagtctcg attgcatcat aattgtgggt tccaaccagc tggacattct 480  
 tacgtatgtt acc 493

<210> 182

<211> 209

<212> PRT

<213> homo sapien

<400> 182

Ala Phe Ser Ser Asn Pro Lys Val Gln Val Glu Ala Ile Glu Gly Gly  
 1 5 10 15  
 Ala Leu Gln Lys Leu Leu Val Ile Leu Ala Thr Glu Gln Pro Leu Thr  
 20 25 30  
 Ala Lys Lys Lys Val Leu Phe Ala Leu Cys Ser Leu Leu Arg His Phe  
 35 40 45  
 Pro Tyr Ala Gln Arg Gln Phe Leu Lys Leu Gly Gly Leu Gln Val Leu  
 50 55 60  
 Arg Thr Leu Val Gln Glu Lys Gly Thr Glu Val Leu Ala Val Arg Val  
 65 70 75 80  
 Val Thr Leu Leu Tyr Asp Leu Val Thr Glu Lys Met Phe Ala Glu Glu  
 85 90 95  
 Glu Ala Glu Leu Thr Gln Glu Met Ser Pro Glu Lys Leu Gln Gln Tyr  
 100 105 110  
 Arg Gln Val His Leu Leu Pro Gly Leu Trp Glu Gln Gly Trp Cys Glu  
 115 120 125  
 Ile Thr Ala His Leu Leu Ala Leu Pro Glu His Asp Ala Arg Glu Lys  
 130 135 140  
 Val Leu Gln Thr Leu Gly Val Leu Leu Thr Thr Cys Arg Asp Arg Tyr  
 145 150 155 160  
 Arg Gln Asp Pro Gln Leu Gly Arg Thr Leu Ala Ser Leu Gln Ala Glu  
 165 170 175  
 Tyr Gln Val Leu Ala Ser Leu Glu Leu Gln Asp Gly Glu Asp Glu Gly  
 180 185 190  
 Tyr Phe Gln Glu Leu Leu Gly Ser Val Asn Ser Leu Leu Lys Glu Leu  
 195 200 205  
 Arg

<210> 183

<211> 255

<212> PRT

<213> homo sapien

<400> 183

Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Pro  
 1 5 10 15

Lys Met Glu Glu Glu Ser Gly Ala Pro Cys Val Pro Ser Gly Asn Gly  
 20 25 30  
 Ala Pro Gly Pro Lys Gly Glu Glu Arg Pro Thr Gln Asn Glu Lys Arg  
 35 40 45  
 Lys Glu Lys Asn Ile Lys Arg Gly Gly Asn Arg Phe Glu Pro Tyr Ser  
 50 55 60  
 Asn Pro Thr Lys Arg Tyr Arg Ala Phe Ile Thr Asn Ile Pro Phe Asp  
 65 70 75 80  
 Val Lys Trp Gln Ser Leu Lys Asp Leu Val Lys Glu Lys Val Gly Glu  
 85 90 95  
 Val Thr Tyr Val Glu Leu Leu Met Asp Ala Glu Gly Lys Ser Arg Gly  
 100 105 110  
 Cys Ala Val Val Glu Phe Lys Met Glu Glu Ser Met Lys Lys Ala Ala  
 115 120 125  
 Glu Val Leu Asn Lys His Ser Leu Ser Gly Arg Pro Leu Lys Val Lys  
 130 135 140  
 Glu Asp Pro Asp Gly Glu His Ala Arg Arg Ala Met Gln Lys Ala Gly  
 145 150 155 160  
 Arg Leu Gly Ser Thr Val Phe Val Ala Asn Leu Asp Tyr Lys Val Gly  
 165 170 175  
 Trp Lys Lys Leu Lys Glu Val Phe Ser Met Ala Gly Val Val Val Arg  
 180 185 190  
 Ala Asp Ile Leu Glu Asp Lys Asp Gly Lys Ser Arg Gly Ile Gly Ile  
 195 200 205  
 Val Thr Phe Glu Gln Ser Ile Glu Ala Val Gln Ala Ile Ser Met Phe  
 210 215 220  
 Asn Gly Gln Leu Leu Phe Asp Arg Pro Met His Val Lys Met Asp Glu  
 225 230 235 240  
 Arg Ala Leu Pro Lys Gly Asp Phe Phe Pro Pro Glu Arg His Ser  
 245 250 255

&lt;210&gt; 184

&lt;211&gt; 188

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 184

Leu Ser Gly Ser Cys Ile Arg Arg Glu Gln Thr Pro Glu Lys Glu Lys  
 1 5 10 15  
 Gln Val Val Leu Phe Glu Glu Ala Ser Trp Thr Cys Thr Pro Ala Cys  
 20 25 30  
 Gly Asp Glu Pro Arg Thr Val Ile Leu Leu Ser Ser Met Leu Ala Asp  
 35 40 45  
 His Arg Leu Lys Leu Glu Asp Tyr Lys Asp Arg Leu Lys Ser Gly Glu  
 50 55 60  
 His Leu Asn Pro Asp Gln Leu Glu Ala Val Glu Lys Tyr Glu Glu Val  
 65 70 75 80  
 Leu His Asn Leu Glu Phe Ala Lys Glu Leu Gln Lys Thr Phe Ser Gly  
 85 90 95  
 Leu Ser Leu Asp Leu Leu Lys Ala Gln Lys Lys Ala Gln Arg Arg Glu  
 100 105 110  
 His Met Leu Lys Leu Glu Ala Glu Lys Lys Lys Leu Arg Thr Ile Leu  
 115 120 125  
 Gln Val Gln Tyr Val Leu Gln Asn Leu Thr Gln Glu His Val Gln Lys  
 130 135 140

Asp Phe Lys Gly Gly Leu Asn Gly Ala Val Tyr Leu Pro Ser Lys Glu  
 145 150 155 160  
 Leu Asp Tyr Leu Ile Lys Phe Ser Lys Leu Thr Cys Pro Glu Arg Asn  
 165 170 175  
 Glu Ser Leu Arg Gln Thr Leu Glu Gly Ser Thr Val  
 180 185

<210> 185  
 <211> 746  
 <212> PRT  
 <213> Homo sapien

<400> 185

Asp Lys His Leu Lys Asp Leu Leu Ser Lys Leu Leu Asn Ser Gly Tyr  
 1 5 10 15  
 Phe Glu Ser Ile Pro Val Pro Lys Asn Ala Lys Glu Lys Glu Val Pro  
 20 25 30  
 Leu Glu Glu Glu Met Leu Ile Gln Ser Glu Lys Lys Thr Gln Leu Ser  
 35 40 45  
 Lys Thr Glu Ser Val Lys Glu Ser Glu Ser Leu Met Glu Phe Ala Gln  
 50 55 60  
 Pro Glu Ile Gln Pro Gln Glu Phe Leu Asn Arg Arg Tyr Met Thr Glu  
 65 70 75 80  
 Val Asp Tyr Ser Asn Lys Gln Gly Glu Glu Gln Pro Trp Glu Ala Asp  
 85 90 95  
 Tyr Ala Arg Lys Pro Asn Leu Pro Lys Arg Trp Asp Met Leu Thr Glu  
 100 105 110  
 Pro Asp Gly Gln Glu Lys Lys Gln Glu Ser Phe Lys Ser Trp Glu Ala  
 115 120 125  
 Ser Gly Lys His Gln Glu Val Ser Lys Pro Ala Val Ser Leu Glu Gln  
 130 135 140  
 Arg Lys Gln Asp Thr Ser Lys Leu Arg Ser Thr Leu Pro Glu Glu Gln  
 145 150 155 160  
 Lys Lys Gln Glu Ile Ser Lys Ser Lys Pro Ser Pro Ser Gln Trp Lys  
 165 170 175  
 Gln Asp Thr Pro Lys Ser Lys Ala Gly Tyr Val Gln Glu Glu Gln Lys  
 180 185 190  
 Lys Gln Glu Thr Pro Lys Leu Trp Pro Val Gln Leu Gln Lys Glu Gln  
 195 200 205  
 Asp Pro Lys Lys Gln Thr Pro Lys Ser Trp Thr Pro Ser Met Gln Ser  
 210 215 220  
 Glu Gln Asn Thr Thr Lys Ser Trp Thr Thr Pro Met Cys Glu Glu Gln  
 225 230 235 240  
 Asp Ser Lys Gln Pro Glu Thr Pro Lys Ser Trp Glu Asn Asn Val Glu  
 245 250 255  
 Ser Gln Lys His Ser Leu Thr Ser Gln Ser Gln Ile Ser Pro Lys Ser  
 260 265 270  
 Trp Gly Val Ala Thr Ala Ser Leu Ile Pro Asn Asp Gln Leu Leu Pro  
 275 280 285  
 Arg Lys Leu Asn Thr Glu Pro Lys Asp Val Pro Lys Pro Val His Gln  
 290 295 300  
 Pro Val Gly Ser Ser Ser Thr Leu Pro Lys Asp Pro Val Leu Arg Lys  
 305 310 315 320  
 Glu Lys Leu Gln Asp Leu Met Thr Gln Ile Gln Gly Thr Cys Asn Phe  
 325 330 335

Met Gln Glu Ser Val Leu Asp Phe Asp Lys Pro Ser Ser Ala Ile Pro  
 340 345 350  
 Thr Ser Gln Pro Pro Ser Ala Thr Pro Gly Ser Pro Val Ala Ser Lys  
 355 360 365  
 Glu Gln Asn Leu Ser Ser Gln Ser Asp Phe Leu Gln Glu Pro Leu Gln  
 370 375 380  
 Val Phe Asn Val Asn Ala Pro Leu Pro Pro Arg Lys Glu Gln Glu Ile  
 385 390 395 400  
 Lys Glu Ser Pro Tyr Ser Pro Gly Tyr Asn Gln Ser Phe Thr Thr Ala  
 405 410 415  
 Ser Thr Gln Thr Pro Pro Gln Cys Gln Leu Pro Ser Ile His Val Glu  
 420 425 430  
 Gln Thr Val His Ser Gln Glu Thr Ala Ala Asn Tyr His Pro Asp Gly  
 435 440 445  
 Thr Ile Gln Val Ser Asn Gly Ser Leu Ala Phe Tyr Pro Ala Gln Thr  
 450 455 460  
 Asn Val Phe Pro Arg Pro Thr Gln Pro Phe Val Asn Ser Arg Gly Ser  
 465 470 475 480  
 Val Arg Gly Cys Thr Arg Gly Gly Arg Leu Ile Thr Asn Ser Tyr Arg  
 485 490 495  
 Ser Pro Gly Gly Tyr Lys Gly Phe Asp Thr Tyr Arg Gly Leu Pro Ser  
 500 505 510  
 Ile Ser Asn Gly Asn Tyr Ser Gln Leu Gln Phe Gln Ala Arg Glu Tyr  
 515 520 525  
 Ser Gly Ala Pro Tyr Ser Gln Arg Asp Asn Phe Gln Gln Cys Tyr Lys  
 530 535 540  
 Arg Gly Gly Thr Ser Gly Gly Pro Arg Ala Asn Ser Arg Ala Gly Trp  
 545 550 555 560  
 Ser Asp Ser Ser Gln Val Ser Ser Pro Glu Arg Asp Asn Glu Thr Phe  
 565 570 575  
 Asn Ser Gly Asp Ser Gly Gln Gly Asp Ser Arg Ser Met Thr Pro Val  
 580 585 590  
 Asp Val Pro Val Thr Asn Pro Ala Ala Thr Ile Leu Pro Val His Val  
 595 600 605  
 Tyr Pro Leu Pro Gln Gln Met Arg Val Ala Phe Ser Ala Ala Arg Thr  
 610 615 620  
 Ser Asn Leu Ala Pro Gly Thr Leu Asp Gln Pro Ile Val Phe Asp Leu  
 625 630 635 640  
 Leu Leu Asn Asn Leu Gly Glu Thr Phe Asp Leu Gln Leu Gly Arg Phe  
 645 650 655  
 Asn Cys Pro Val Asn Gly Thr Tyr Val Phe Ile Phe His Met Leu Lys  
 660 665 670  
 Leu Ala Val Asn Val Pro Leu Tyr Val Asn Leu Met Lys Asn Glu Glu  
 675 680 685  
 Val Leu Val Ser Ala Tyr Ala Asn Asp Gly Ala Pro Asp His Glu Thr  
 690 695 700  
 Ala Ser Asn His Ala Ile Leu Gln Leu Phe Gln Gly Asp Gln Ile Trp  
 705 710 715 720  
 Leu Arg Leu His Arg Gly Ala Ile Tyr Gly Ser Ser Trp Lys Tyr Ser  
 725 730 735  
 Thr Phe Ser Gly Tyr Leu Leu Tyr Gln Asp  
 740 745

&lt;210&gt; 186

&lt;211&gt; 705

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 186

Ala Leu Leu Asn Val Arg Gln Pro Pro Ser Thr Thr Thr Phe Val Leu  
 1 5 10 15  
 Asn Gln Ile Asn His Leu Pro Pro Leu Gly Ser Thr Ile Val Met Thr  
 20 25 30  
 Lys Thr Pro Pro Val Thr Thr Asn Arg Gln Thr Ile Thr Leu Thr Lys  
 35 40 45  
 Phe Ile Gln Thr Thr Ala Ser Thr Arg Pro Ser Val Ser Ala Pro Thr  
 50 55 60  
 Val Arg Asn Ala Met Thr Ser Ala Pro Ser Lys Asp Gln Val Gln Leu  
 65 70 75 80  
 Lys Asp Leu Leu Lys Asn Asn Ser Leu Asn Glu Leu Met Lys Leu Lys  
 85 90 95  
 Pro Pro Ala Asn Ile Ala Gln Pro Val Ala Thr Ala Ala Thr Asp Val  
 100 105 110  
 Ser Asn Gly Thr Val Lys Lys Glu Ser Ser Asn Lys Glu Gly Ala Arg  
 115 120 125  
 Met Trp Ile Asn Asp Met Lys Met Arg Ser Phe Ser Pro Thr Met Lys  
 130 135 140  
 Val Pro Val Val Lys Glu Asp Asp Glu Pro Glu Glu Asp Glu Glu  
 145 150 155 160  
 Glu Met Gly His Ala Glu Thr Tyr Ala Glu Tyr Met Pro Ile Lys Leu  
 165 170 175  
 Lys Ile Gly Leu Arg His Pro Asp Ala Val Val Glu Thr Ser Ser Leu  
 180 185 190  
 Ser Ser Val Thr Pro Pro Asp Val Trp Tyr Lys Thr Ser Ile Ser Glu  
 195 200 205  
 Glu Thr Ile Asp Asn Gly Trp Leu Ser Ala Leu Gln Leu Glu Ala Ile  
 210 215 220  
 Thr Tyr Ala Ala Gln Gln His Glu Thr Phe Leu Pro Asn Gly Asp Arg  
 225 230 235 240  
 Ala Gly Phe Leu Ile Gly Asp Gly Ala Gly Val Gly Lys Gly Arg Thr  
 245 250 255  
 Ile Ala Gly Ile Ile Tyr Glu Asn Tyr Leu Leu Ser Arg Lys Arg Ala  
 260 265 270  
 Leu Trp Phe Ser Val Ser Asn Asp Leu Lys Tyr Asp Ala Glu Arg Asp  
 275 280 285  
 Leu Arg Asp Ile Gly Ala Lys Asn Ile Leu Val His Ser Leu Asn Lys  
 290 295 300  
 Phe Lys Tyr Gly Lys Ile Ser Ser Lys His Asn Gly Ser Val Lys Lys  
 305 310 315 320  
 Gly Val Ile Phe Ala Thr Tyr Ser Ser Leu Ile Gly Glu Ser Gln Ser  
 325 330 335  
 Gly Gly Lys Tyr Lys Thr Arg Leu Lys Gln Leu Leu His Trp Cys Gly  
 340 345 350  
 Asp Asp Phe Asp Gly Val Ile Val Phe Asp Glu Cys His Lys Ala Lys  
 355 360 365  
 Asn Leu Cys Pro Val Gly Ser Ser Lys Pro Thr Lys Thr Gly Leu Ala  
 370 375 380  
 Val Leu Glu Leu Gln Asn Lys Leu Pro Lys Ala Arg Val Val Tyr Ala  
 385 390 395 400  
 Ser Ala Thr Gly Ala Ser Glu Pro Arg Asn Met Ala Tyr Met Asn Arg

405 410 415  
 Leu Gly Ile Trp Gly Glu Gly Thr Pro Phe Arg Glu Phe Ser Asp Phe  
 420 425 430  
 Ile Gln Ala Val Glu Arg Arg Gly Val Gly Ala Met Glu Ile Val Ala  
 435 440 445  
 Met Asp Met Lys Leu Arg Gly Met Tyr Ile Ala Arg Gln Leu Ser Phe  
 450 455 460  
 Thr Gly Val Thr Phe Lys Ile Glu Glu Val Leu Leu Ser Gln Ser Tyr  
 465 470 475 480  
 Val Lys Met Tyr Asn Lys Ala Val Lys Leu Trp Val Ile Ala Arg Glu  
 485 490 495  
 Arg Phe Gln Gln Ala Ala Asp Leu Ile Asp Ala Glu Gln Arg Met Lys  
 500 505 510  
 Lys Ser Met Trp Gly Gln Phe Trp Ser Ala His Gln Arg Phe Phe Lys  
 515 520 525  
 Tyr Leu Cys Ile Ala Ser Lys Val Lys Arg Val Val Gln Leu Ala Arg  
 530 535 540  
 Glu Glu Ile Lys Asn Gly Lys Cys Val Val Ile Gly Leu Gln Ser Thr  
 545 550 555 560  
 Gly Glu Ala Arg Thr Leu Glu Ala Leu Glu Glu Gly Gly Gly Glu Leu  
 565 570 575  
 Asn Asp Phe Val Ser Thr Ala Lys Gly Val Leu Gln Ser Leu Ile Glu  
 580 585 590  
 Lys His Phe Pro Ala Pro Asp Arg Lys Lys Leu Tyr Ser Leu Leu Gly  
 595 600 605  
 Ile Asp Leu Thr Ala Pro Ser Asn Asn Ser Ser Pro Arg Asp Ser Pro  
 610 615 620  
 Cys Lys Glu Asn Lys Ile Lys Lys Arg Lys Gly Glu Glu Ile Thr Arg  
 625 630 635 640  
 Glu Ala Lys Lys Ala Arg Lys Val Gly Gly Leu Thr Gly Ser Ser Ser  
 645 650 655  
 Asp Asp Ser Gly Ser Glu Ser Asp Ala Ser Asp Asn Glu Glu Ser Asp  
 660 665 670  
 Tyr Glu Ser Ser Lys Asn Met Ser Ser Gly Asp Asp Asp Phe Asn  
 675 680 685  
 Pro Phe Leu Asp Glu Ser Asn Glu Asp Asp Glu Asn Asp Pro Trp Leu  
 690 695 700  
 Ile  
 705

<210> 187  
 <211> 595  
 <212> PRT  
 <213> Homo sapien

<400> 187  
 Glu Ser Pro Arg His Arg Gly Glu Gly Gly Glu Trp Gly Pro Gly  
 1 5 10 15  
 Val Pro Arg Glu Arg Arg Glu Ser Ala Gly Glu Trp Gly Ala Asp Thr  
 20 25 30  
 Pro Lys Glu Gly Gly Glu Ser Ala Gly Glu Trp Gly Ala Glu Val Pro  
 35 40 45  
 Arg Gly Arg Gly Glu Gly Ala Gly Glu Trp Gly Pro Asp Thr Pro Lys  
 50 55 60  
 Glu Arg Gly Gln Gly Val Arg Glu Trp Gly Pro Glu Ile Pro Gln Glu

65                      70                      75                      80  
 His Gly Glu Ala Thr Arg Asp Trp Ala Leu Glu Ser Pro Arg Ala Leu  
                                  85                      90                      95  
 Gly Glu Asp Ala Arg Glu Leu Gly Ser Ser Pro His Asp Arg Gly Ala  
                                  100                      105                      110  
 Ser Pro Arg Asp Leu Ser Gly Glu Ser Pro Cys Thr Gln Arg Ser Gly  
                                  115                      120                      125  
 Leu Leu Pro Glu Arg Arg Gly Asp Ser Pro Trp Pro Trp Pro Ser  
                                  130                      135                      140  
 Pro Gln Glu Arg Asp Ala Gly Thr Arg Asp Arg Glu Glu Ser Pro Arg  
 145                      150                      155                      160  
 Asp Trp Gly Gly Ala Glu Ser Pro Arg Gly Trp Glu Ala Gly Pro Arg  
                                  165                      170                      175  
 Glu Trp Gly Pro Ser Pro Ser Gly His Gly Asp Gly Pro Arg Arg Arg  
                                  180                      185                      190  
 Pro Arg Lys Arg Arg Gly Arg Lys Gly Arg Met Gly Arg Gln His Glu  
                                  195                      200                      205  
 Ala Ala Ala Thr Ala Ala Thr Ala Ala Thr Ala Thr Gly Gly Thr Ala  
                                  210                      215                      220  
 Glu Glu Ala Gly Ala Ser Ala Pro Glu Ser Gln Ala Gly Gly Gly Pro  
 225                      230                      235                      240  
 Arg Gly Arg Ala Arg Gly Pro Arg Gln Gln Gly Arg Arg Arg His Gly  
                                  245                      250                      255  
 Thr Gln Arg Arg Arg Gly Pro Pro Gln Ala Arg Glu Glu Gly Pro Arg  
                                  260                      265                      270  
 Asp Ala Thr Thr Ile Leu Gly Leu Gly Thr Pro Ser Gly Glu Gln Arg  
                                  275                      280                      285  
 Ala Asp Gln Ser Gln Ala Leu Pro Ala Leu Ala Gly Ala Ala Ala Ala  
                                  290                      295                      300  
 His Ala His Ala Ile Pro Gly Ala Gly Pro Ala Ala Ala Pro Val Gly  
 305                      310                      315                      320  
 Gly Arg Gly Arg Arg Gly Gly Trp Arg Gly Gly Arg Arg Gly Gly Ser  
                                  325                      330                      335  
 Ala Gly Ala Gly Gly Gly Gly Arg Gly Gly Arg Gly Arg Gly Arg Gly  
                                  340                      345                      350  
 Gly Gly Arg Gly Gly Gly Gly Ala Gly Arg Gly Gly Gly Ala Ala Gly  
                                  355                      360                      365  
 Pro Arg Glu Gly Ala Ser Ser Pro Gly Ala Arg Arg Gly Glu Gln Arg  
                                  370                      375                      380  
 Arg Arg Gly Arg Gly Pro Pro Ala Ala Gly Ala Ala Gln Val Ser Ala  
 385                      390                      395                      400  
 Arg Gly Arg Arg Ala Arg Gly Gln Arg Ala Gly Glu Glu Ala Gln Asp  
                                  405                      410                      415  
 Gly Leu Leu Pro Arg Gly Arg Asp Arg Leu Pro Leu Arg Pro Gly Asp  
                                  420                      425                      430  
 Ala Asn Gln Arg Ala Glu Arg Pro Gly Pro Pro Arg Gly Gly His Gly  
                                  435                      440                      445  
 Pro Val Asn Ala Ser Ser Ala Pro Asp Thr Ser Pro Pro Arg His Pro  
                                  450                      455                      460  
 Arg Arg Trp Val Ser Gln Arg Gln Arg Leu Trp Arg Gln Phe Arg  
 465                      470                      475                      480  
 Val Gly Gly Gly Phe Pro Pro Pro Pro Pro Ser Arg Pro Pro Ala Val  
                                  485                      490                      495  
 Leu Leu Pro Leu Leu Arg Leu Ala Cys Ala Gly Asp Pro Gly Ala Thr  
                                  500                      505                      510



Arg Pro Gly Pro Arg Arg Pro Ala Arg Arg Pro Arg Gly Glu Leu Ile  
 515 520 525  
 Pro Arg Arg Pro Asp Pro Ala Ala Pro Ser Glu Glu Gly Leu Arg Met  
 530 535 540  
 Glu Ser Ser Val Asp Asp Gly Ala Thr Ala Thr Thr Ala Asp Ala Ala  
 545 550 555 560  
 Ser Gly Glu Ala Pro Glu Ala Gly Pro Ser Pro Ser His Ser Pro Thr  
 565 570 575  
 Met Cys Gln Thr Gly Gly Pro Gly Pro Pro Pro Pro Gln Pro Pro Arg  
 580 585 590  
 Trp Leu Pro  
 595

<210> 188  
 <211> 376  
 <212> PRT  
 <213> Homo sapien

<400> 188

Glu Met Arg Lys Phe Asp Val Pro Ser Met Glu Ser Thr Leu Asn Gln  
 1 5 10 15  
 Pro Ala Met Leu Glu Thr Leu Tyr Ser Asp Pro His Tyr Arg Ala His  
 20 25 30  
 Phe Pro Asn Pro Arg Pro Asp Thr Asn Lys Asp Val Tyr Lys Val Leu  
 35 40 45  
 Pro Glu Ser Lys Lys Ala Pro Gly Ser Gly Ala Val Phe Glu Arg Asn  
 50 55 60  
 Gly Pro His Ala Ser Ser Ser Gly Val Leu Pro Leu Gly Leu Gln Pro  
 65 70 75 80  
 Ala Pro Gly Leu Ser Lys Ser Leu Ser Ser Gln Val Trp Gln Pro Ser  
 85 90 95  
 Pro Asp Pro Trp His Pro Gly Glu Gln Ser Cys Glu Leu Ser Thr Cys  
 100 105 110  
 Arg Gln Gln Leu Glu Leu Ile Arg Leu Gln Met Glu Gln Met Gln Leu  
 115 120 125  
 Gln Asn Gly Ala Met Cys His His Pro Ala Ala Phe Ala Pro Leu Leu  
 130 135 140  
 Pro Thr Leu Glu Pro Ala Gln Trp Leu Ser Ile Leu Asn Ser Asn Glu  
 145 150 155 160  
 His Leu Leu Lys Glu Lys Glu Leu Leu Ile Asp Lys Gln Arg Lys His  
 165 170 175  
 Ile Ser Gln Leu Glu Gln Lys Val Arg Glu Ser Glu Leu Gln Val His  
 180 185 190  
 Ser Ala Leu Leu Gly Arg Pro Ala Pro Phe Gly Asp Val Cys Leu Leu  
 195 200 205  
 Arg Leu Gln Glu Leu Gln Arg Glu Asn Thr Phe Leu Arg Ala Gln Phe  
 210 215 220  
 Ala Gln Lys Thr Glu Ala Leu Ser Lys Glu Lys Met Glu Leu Glu Lys  
 225 230 235 240  
 Lys Leu Ser Ala Ser Glu Val Glu Ile Gln Leu Ile Arg Glu Ser Leu  
 245 250 255  
 Lys Val Thr Leu Gln Lys His Ser Glu Glu Gly Lys Lys Gln Glu Glu  
 260 265 270  
 Arg Val Lys Gly Arg Asp Lys His Ile Asn Asn Leu Lys Lys Lys Cys  
 275 280 285

Gln Lys Glu Ser Glu Gln Asn Arg Glu Lys Gln Gln Arg Ile Glu Thr  
 290 295 300  
 Leu Glu Arg Tyr Leu Ala Asp Leu Pro Thr Leu Glu Asp His Gln Lys  
 305 310 315 320  
 Gln Thr Glu Gln Leu Lys Asp Ala Glu Leu Lys Asn Thr Glu Leu Gln  
 325 330 335  
 Glu Arg Val Ala Glu Leu Glu Thr Leu Leu Glu Asp Thr Gln Ala Thr  
 340 345 350  
 Cys Arg Glu Lys Glu Val Gln Leu Glu Ser Leu Arg Gln Arg Glu Ala  
 355 360 365  
 Asp Leu Ser Ser Ala Arg His Arg  
 370 375

<210> 189  
 <211> 160  
 <212> PRT  
 <213> Homo sapien

<400> 189  
 Met Leu Glu Ala His Arg Arg Gln Arg His Pro Phe Leu Leu Leu Gly  
 1 5 10 15  
 Thr Thr Ala Asn Arg Thr Gln Ser Leu Asn Tyr Gly Cys Ile Val Glu  
 20 25 30  
 Asn Pro Gln Thr His Glu Val Leu His Tyr Val Glu Lys Pro Ser Thr  
 35 40 45  
 Phe Ile Ser Asp Ile Ile Asn Cys Gly Ile Tyr Leu Phe Ser Pro Glu  
 50 55 60  
 Ala Leu Lys Pro Leu Arg Asp Val Phe Gln Arg Asn Gln Gln Asp Gly  
 65 70 75 80  
 Gln Leu Glu Asp Ser Pro Gly Leu Trp Pro Gly Ala Gly Thr Ile Arg  
 85 90 95  
 Leu Glu Gln Asp Val Phe Ser Ala Leu Ala Gly Gln Gly Gln Ile Tyr  
 100 105 110  
 Val His Leu Thr Asp Gly Ile Trp Ser Gln Ile Lys Ser Ala Gly Ser  
 115 120 125  
 Ala Leu Tyr Ala Ser Arg Leu Tyr Leu Ser Arg Tyr Gln Asp Thr His  
 130 135 140  
 Pro Glu Arg Leu Ala Lys His Thr Pro Gly Gly Pro Trp Ile Arg Gly  
 145 150 155 160

<210> 190  
 <211> 146  
 <212> PRT  
 <213> Homo sapien

<400> 190  
 Met Asp Pro Arg Ala Ser Leu Leu Leu Leu Gly Asn Val Tyr Ile His  
 1 5 10 15  
 Pro Thr Ala Lys Val Ala Pro Ser Ala Val Leu Gly Pro Asn Val Ser  
 20 25 30  
 Ile Gly Lys Gly Val Thr Val Gly Glu Gly Val Arg Leu Arg Glu Ser  
 35 40 45  
 Ile Val Leu His Gly Ala Thr Leu Gln Glu His Thr Cys Val Leu His  
 50 55 60  
 Ser Ile Val Gly Trp Gly Ser Thr Val Gly Arg Trp Ala Arg Val Glu

<210> 191  
<211> 704  
<212> PRT  
<213> Homo sapien

<sup>400> 191</sup>  
 Glu Gly Gly Cys Ala Ala Gly Arg Gly Arg Glu Leu Glu Pro Glu Leu  
 1 5 10 15  
 Glu Pro Gly Pro Gly Pro Gly Ser Ala Leu Glu Pro Gly Glu Glu Phe  
 20 25 30  
 Glu Ile Val Asp Arg Ser Gln Leu Pro Gly Pro Gly Asp Leu Arg Ser  
 35 40 45  
 Ala Thr Arg Pro Arg Ala Ala Glu Gly Trp Ser Ala Pro Ile Leu Thr  
 50 55 60  
 Leu Ala Arg Arg Ala Thr Gly Asn Leu Ser Ala Ser Cys Gly Ser Ala  
 65 70 75 80  
 Leu Arg Ala Ala Ala Gly Leu Gly Gly Asp Ser Gly Asp Gly Thr  
 85 90 95  
 Ala Arg Ala Ala Ser Lys Cys Gln Met Met Glu Glu Arg Ala Asn Leu  
 100 105 110  
 Met His Met Met Lys Leu Ser Ile Lys Val Leu Leu Gln Ser Ala Leu  
 115 120 125  
 Ser Leu Gly Arg Ser Leu Asp Ala Asp His Ala Pro Leu Gln Gln Phe  
 130 135 140  
 Phe Val Val Met Glu His Cys Leu Lys His Gly Leu Lys Val Lys Lys  
 145 150 155 160  
 Ser Phe Ile Gly Gln Asn Lys Ser Phe Phe Gly Pro Leu Glu Leu Val  
 165 170 175  
 Glu Lys Leu Cys Pro Glu Ala Ser Asp Ile Ala Thr Ser Val Arg Asn  
 180 185 190  
 Leu Pro Glu Leu Lys Thr Ala Val Gly Arg Gly Arg Ala Trp Leu Tyr  
 195 200 205  
 Leu Ala Leu Met Gln Lys Lys Leu Ala Asp Tyr Leu Lys Val Leu Ile  
 210 215 220  
 Asp Asn Lys His Leu Leu Ser Glu Phe Tyr Glu Pro Glu Ala Leu Met  
 225 230 235 240  
 Met Glu Glu Glu Gly Met Val Ile Val Gly Leu Leu Val Gly Leu Asn  
 245 250 255  
 Val Leu Asp Ala Asn Leu Cys Leu Lys Gly Glu Asp Leu Asp Ser Gln  
 260 265 270  
 Val Gly Val Ile Asp Phe Ser Leu Tyr Leu Lys Asp Val Gln Asp Leu  
 275 280 285  
 Asp Gly Gly Lys Glu His Glu Arg Ile Thr Asp Val Leu Asp Gln Lys

290  
 Asn Tyr Val Glu Glu Leu Asn Arg His Leu Ser Cys Thr Val Gly Asp  
 305 310 315 320  
 Leu Gln Thr Lys Ile Asp Gly Leu Glu Lys Thr Asn Ser Lys Leu Gln  
 325 330 335  
 Glu Glu Leu Ser Ala Ala Thr Asp Arg Ile Cys Ser Leu Gln Glu  
 340 345 350  
 Gln Gln Gln Leu Arg Glu Gln Asn Glu Leu Ile Arg Glu Arg Ser Glu  
 355 360 365  
 Lys Ser Val Glu Ile Thr Lys Gln Asp Thr Lys Val Glu Leu Glu Thr  
 370 375 380  
 Tyr Lys Gln Thr Arg Gln Gly Leu Asp Glu Met Tyr Ser Asp Val Trp  
 385 390 395 400  
 Lys Gln Leu Lys Glu Glu Lys Lys Val Arg Leu Glu Leu Glu Lys Glu  
 405 410 415  
 Leu Glu Leu Gln Ile Gly Met Lys Thr Glu Met Glu Ile Ala Met Lys  
 420 425 430  
 Leu Leu Glu Lys Asp Thr His Glu Lys Gln Asp Thr Leu Val Ala Leu  
 435 440 445  
 Arg Gln Gln Leu Glu Glu Val Lys Ala Ile Asn Leu Gln Met Phe His  
 450 455 460  
 Lys Ala Gln Asn Ala Glu Ser Ser Leu Gln Gln Lys Asn Glu Ala Ile  
 465 470 475 480  
 Thr Ser Phe Glu Gly Lys Thr Asn Gln Val Met Ser Ser Met Lys Gln  
 485 490 495  
 Met Glu Glu Arg Leu Gln His Ser Glu Arg Ala Arg Gln Gly Ala Glu  
 500 505 510  
 Glu Arg Ser His Lys Leu Gln Gln Glu Leu Gly Gly Arg Ile Gly Ala  
 515 520 525  
 Leu Gln Leu Gln Leu Ser Gln Leu His Glu Gln Cys Ser Ser Leu Glu  
 530 535 540  
 Lys Glu Leu Lys Ser Glu Lys Glu Gln Arg Gln Ala Leu Gln Arg Glu  
 545 550 555 560  
 Leu Gln His Glu Lys Asp Thr Ser Ser Leu Leu Arg Met Glu Leu Gln  
 565 570 575  
 Gln Val Glu Gly Leu Lys Lys Glu Leu Arg Glu Leu Gln Asp Glu Lys  
 580 585 590  
 Ala Glu Leu Gln Lys Ile Cys Glu Glu Gln Glu Gln Ala Leu Gln Glu  
 595 600 605  
 Met Gly Leu His Leu Ser Gln Ser Lys Leu Lys Met Glu Asp Ile Lys  
 610 615 620  
 Glu Val Asn Gln Ala Leu Lys Gly His Ala Trp Leu Lys Asp Asp Glu  
 625 630 635 640  
 Ala Thr His Cys Arg Gln Cys Glu Lys Glu Phe Ser Ile Ser Arg Arg  
 645 650 655  
 Lys His His Cys Arg Asn Cys Gly His Ile Phe Cys Asn Thr Cys Ser  
 660 665 670  
 Ser Asn Glu Leu Ala Leu Pro Ser Tyr Pro Lys Pro Val Arg Val Cys  
 675 680 685  
 Asp Ser Cys His Thr Leu Leu Gln Arg Cys Ser Ser Thr Ala Ser  
 690 695 700

&lt;210&gt; 192

&lt;211&gt; 331

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 192

Arg Ala Gly Ala Ser Ala Met Ala Leu Arg Lys Glu Leu Leu Lys Ser  
 1 5 10 15  
 Ile Trp Tyr Ala Phe Thr Ala Leu Asp Val Glu Lys Ser Gly Lys Val  
 20 25 30  
 Ser Lys Ser Gln Leu Lys Val Leu Ser His Asn Leu Tyr Thr Val Leu  
 35 40 45  
 His Ile Pro His Asp Pro Val Ala Leu Glu Glu His Phe Arg Asp Asp  
 50 55 60  
 Asp Asp Gly Pro Val Ser Ser Gln Gly Tyr Met Pro Tyr Leu Asn Lys  
 65 70 75 80  
 Tyr Ile Leu Asp Lys Val Glu Glu Gly Ala Phe Val Lys Glu His Phe  
 85 90 95  
 Asp Glu Leu Cys Trp Thr Leu Thr Ala Lys Lys Asn Tyr Arg Ala Asp  
 100 105 110  
 Ser Asn Gly Asn Ser Met Leu Ser Asn Gln Asp Ala Phe Arg Leu Trp  
 115 120 125  
 Cys Leu Phe Asn Phe Leu Ser Glu Asp Lys Tyr Pro Leu Ile Met Val  
 130 135 140  
 Pro Asp Glu Val Glu Tyr Leu Leu Lys Lys Val Leu Ser Ser Met Ser  
 145 150 155 160  
 Leu Glu Val Ser Leu Gly Glu Leu Glu Glu Leu Ala Gln Glu Ala  
 165 170 175  
 Gln Val Ala Gln Thr Thr Gly Gly Leu Ser Val Trp Gln Phe Leu Glu  
 180 185 190  
 Leu Phe Asn Ser Gly Arg Cys Leu Arg Gly Val Gly Arg Asp Thr Leu  
 195 200 205  
 Ser Met Ala Ile His Glu Val Tyr Gln Glu Leu Ile Gln Asp Val Leu  
 210 215 220  
 Lys Gln Gly Tyr Leu Trp Lys Arg Gly His Leu Arg Arg Asn Trp Ala  
 225 230 235 240  
 Glu Arg Trp Phe Gln Leu Gln Pro Ser Cys Leu Cys Tyr Phe Gly Ser  
 245 250 255  
 Glu Glu Cys Lys Glu Lys Arg Gly Ile Ile Pro Leu Asp Ala His Cys  
 260 265 270  
 Cys Val Glu Val Leu Pro Asp Arg Asp Gly Lys Arg Cys Met Phe Cys  
 275 280 285  
 Val Lys Thr Ala Thr Arg Thr Tyr Glu Met Ser Ala Ser Asp Thr Arg  
 290 295 300  
 Gln Arg Gln Glu Trp Thr Ala Ala Ile Gln Met Ala Ile Arg Leu Gln  
 305 310 315 320  
 Ala Glu Gly Lys Thr Ser Leu His Lys Asp Leu  
 325 330

&lt;210&gt; 193

&lt;211&gt; 475

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 193

Lys Asn Ser Pro Leu Leu Ser Val Ser Ser Gln Thr Ile Thr Lys Glu  
 1 5 10 15  
 Asn Asn Arg Asn Val His Leu Glu His Ser Glu Gln Asn Pro Gly Ser

20	25	30
Ser Ala Gly Asp Thr Ser Ala	Ala His Gln Val Val Leu Gly Glu Asn	
35	40	45
Leu Ile Ala Thr Ala Leu Cys	Leu Ser Gly Ser Gly Ser Gln Ser Asp	
50	55	60
Leu Lys Asp Val Ala Ser Thr	Ala Gly Glu Glu Gly Asp Thr Ser Leu	
65	70	75
Arg Glu Ser Leu His Pro Val	Thr Arg Ser Leu Lys Ala Gly Cys His	
85	90	95
Thr Lys Gln Leu Ala Ser Arg	Asn Cys Ser Glu Glu Lys Ser Pro Gln	
100	105	110
Thr Ser Ile Leu Lys Glu Gly	Asn Arg Asp Thr Ser Leu Asp Phe Arg	
115	120	125
Pro Val Val Ser Pro Ala Asn	Gly Val Glu Gly Val Arg Val Asp Gln	
130	135	140
Asp Asp Asp Gln Asp Ser Ser	Ser Leu Lys Leu Ser Gln Asn Ile Ala	
145	150	155
Val Gln Thr Asp Phe Lys Thr	Ala Asp Ser Glu Val Asn Thr Asp Gln	
165	170	175
Asp Ile Glu Lys Asn Leu Asp	Lys Met Met Thr Glu Arg Thr Leu Leu	
180	185	190
Lys Glu Arg Tyr Gln Glu Val	Leu Asp Lys Gln Arg Gln Val Glu Asn	
195	200	205
Gln Leu Gln Val Gln Leu Lys	Gln Leu Gln Gln Arg Arg Glu Glu Glu	
210	215	220
Met Lys Asn His Gln Glu Ile	Leu Lys Ala Ile Gln Asp Val Thr Ile	
225	230	235
Lys Arg Glu Glu Thr Lys Lys	Lys Ile Glu Lys Glu Lys Lys Glu Phe	
245	250	255
Leu Gln Lys Glu Gln Asp Leu	Lys Ala Glu Ile Glu Lys Leu Cys Glu	
260	265	270
Lys Gly Arg Arg Glu Val Trp	Glu Met Glu Leu Asp Arg Leu Lys Asn	
275	280	285
Gln Asp Gly Glu Ile Asn Arg	Asn Ile Met Glu Glu Thr Glu Arg Ala	
290	295	300
Trp Lys Ala Glu Ile Leu Ser	Leu Glu Ser Arg Lys Glu Leu Leu Val	
305	310	315
Leu Lys Leu Glu Glu Ala Glu	Lys Glu Ala Glu Leu His Leu Thr Tyr	
325	330	335
Leu Lys Ser Thr Pro Pro Thr	Leu Glu Thr Val Arg Ser Lys Gln Glu	
340	345	350
Trp Glu Thr Arg Leu Asn Gly	Val Arg Ile Met Lys Lys Asn Val Arg	
355	360	365
Asp Gln Phe Asn Ser His Ile	Gln Leu Val Arg Asn Gly Ala Lys Leu	
370	375	380
Ser Ser Leu Pro Gln Ile Pro	Thr Pro Thr Leu Pro Pro Pro Pro Ser	
385	390	395
Glu Thr Asp Phe Met Leu Gln	Val Phe Gln Pro Ser Pro Ser Leu Ala	
405	410	415
Pro Arg Met Pro Phe Ser Ile	Gly Gln Val Thr Met Pro Met Val Met	
420	425	430
Pro Ser Ala Asp Pro Arg Ser	Leu Ser Phe Pro Ile Leu Asn Pro Ala	
435	440	445
Leu Ser Gln Pro Ser Gln Pro	Ser Ser Pro Leu Pro Gly Ser His Gly	
450	455	460

Arg Asn Ser Pro Gly Leu Gly Ser Leu Val Ser  
465 470 475

<210> 194  
<211> 241  
<212> PRT  
<213> Homo sapien

<400> 194

Met Ser Gly Glu Ser Ala Arg Ser Leu Gly Lys Gly Ser Ala Pro Pro  
1 5 10 15  
Gly Pro Val Pro Glu Gly Ser Ile Arg Ile Tyr Ser Met Arg Phe Cys  
20 25 30  
Pro Phe Ala Glu Arg Thr Arg Leu Val Leu Lys Ala Lys Gly Ile Arg  
35 40 45  
His Glu Val Ile Asn Ile Asn Leu Lys Asn Lys Pro Glu Trp Phe Phe  
50 55 60  
Lys Lys Asn Pro Phe Gly Leu Val Pro Val Leu Glu Asn Ser Gln Gly  
65 70 75 80  
Gln Leu Ile Tyr Glu Ser Ala Ile Thr Cys Glu Tyr Leu Asp Glu Ala  
85 90 95  
Tyr Pro Gly Lys Lys Leu Leu Pro Asp Asp Pro Tyr Glu Lys Ala Cys  
100 105 110  
Gln Lys Met Ile Leu Glu Leu Phe Ser Lys Val Pro Ser Leu Val Gly  
115 120 125  
Ser Phe Ile Arg Ser Gln Asn Lys Glu Asp Tyr Ala Gly Leu Lys Glu  
130 135 140  
Glu Phe Arg Lys Glu Phe Thr Lys Leu Glu Glu Val Leu Thr Asn Lys  
145 150 155 160  
Lys Thr Thr Phe Phe Gly Gly Asn Ser Ile Ser Met Ile Asp Tyr Leu  
165 170 175  
Ile Trp Pro Trp Phe Glu Arg Leu Glu Ala Met Lys Leu Asn Glu Cys  
180 185 190  
Val Asp His Thr Pro Lys Leu Lys Leu Trp Met Ala Ala Met Lys Glu  
195 200 205  
Asp Pro Thr Val Ser Ala Leu Leu Thr Ser Glu Lys Asp Trp Gln Gly  
210 215 220  
Phe Leu Glu Leu Tyr Leu Gln Asn Ser Pro Glu Ala Cys Asp Tyr Gly  
225 230 235 240  
Leu

<210> 195  
<211> 138  
<212> PRT  
<213> Homo sapien

<400> 195

Gln Thr Lys Ile Leu Glu Glu Asp Leu Glu Gln Ile Lys Leu Ser Leu  
1 5 10 15  
Arg Glu Arg Gly Arg Glu Leu Thr Thr Gln Arg Gln Leu Met Gln Glu  
20 25 30  
Arg Ala Glu Glu Gly Lys Gly Pro Ser Lys Ala Gln Arg Gly Ser Leu  
35 40 45  
Glu His Met Lys Leu Ile Leu Arg Asp Lys Glu Lys Glu Val Glu Cys

50                      55                      60  
 Gln Gln Glu His Ile His Glu Leu Gln Glu Leu Lys Asp Gln Leu Glu  
 65                      70                      75                      80  
 Gln Gln Leu Gln Gly Leu His Arg Lys Val Gly Glu Thr Ser Leu Leu  
                     85                      90                      95  
 Leu Ser Gln Arg Glu Gln Glu Ile Val Val Leu Gln Gln Gln Leu Gln  
                     100                      105                      110  
 Glu Ala Arg Glu Gln Gly Glu Leu Lys Glu Gln Ser Leu Gln Ser Gln  
                     115                      120                      125  
 Leu Asp Glu Ala Gln Arg Ala Leu Ala Gln  
                     130                      135

&lt;210&gt; 196

&lt;211&gt; 102

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 196

Met Ser Lys Arg Lys Ala Pro Gln Glu Thr Leu Asn Gly Gly Ile Thr  
 1                      5                      10                      15  
 Asp Met Leu Thr Glu Leu Ala Asn Phe Glu Lys Asn Val Ser Gln Ala  
                     20                      25                      30  
 Ile His Lys Tyr Asn Ala Tyr Arg Lys Ala Ala Ser Val Ile Ala Lys  
                     35                      40                      45  
 Tyr Pro His Lys Ile Lys Ser Gly Ala Glu Ala Lys Lys Leu Pro Gly  
                     50                      55                      60  
 Val Gly Thr Lys Ile Ala Glu Lys Ile Asp Glu Phe Leu Ala Thr Gly  
 65                      70                      75                      80  
 Lys Leu Arg Lys Leu Glu Lys Ile Arg Gln Asp Asp Thr Ser Ser Ser  
                     85                      90                      95  
 Ile Asn Phe Leu Thr Arg  
                     100

&lt;210&gt; 197

&lt;211&gt; 138

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 197

Glu Ala Asn Glu Val Thr Asp Ser Ala Tyr Met Gly Ser Glu Ser Thr  
 1                      5                      10                      15  
 Tyr Ser Glu Cys Glu Thr Phe Thr Asp Glu Asp Thr Ser Thr Leu Val  
                     20                      25                      30  
 His Pro Glu Leu Gln Pro Glu Gly Asp Ala Asp Ser Ala Gly Gly Ser  
                     35                      40                      45  
 Ala Val Pro Ser Glu Cys Leu Asp Ala Met Glu Glu Pro Asp His Gly  
                     50                      55                      60  
 Ala Leu Leu Leu Leu Pro Gly Arg Pro His Pro His Gly Gln Ser Val  
 65                      70                      75                      80  
 Ile Thr Val Ile Gly Gly Glu Glu His Phe Glu Asp Tyr Gly Glu Gly  
                     85                      90                      95  
 Ser Glu Ala Glu Leu Ser Pro Glu Thr Leu Cys Asn Gly Gln Leu Gly  
                     100                      105                      110  
 Cys Ser Asp Pro Ala Phe Leu Thr Pro Ser Pro Thr Lys Arg Leu Ser  
                     115                      120                      125



Ser Lys Lys Val Ala Arg Tyr Leu His Gln  
130 135

<210> 198  
<211> 100  
<212> PRT  
<213> Homo sapien

<400> 198

Met Gly Asp Val Lys Asn Phe Leu Tyr Ala Trp Cys Gly Lys Arg Lys  
1 5 10 15  
Met Thr Pro Ser Tyr Glu Ile Arg Ala Val Gly Asn Lys Asn Arg Gln  
20 25 30  
Lys Phe Met Cys Glu Val Gln Val Glu Gly Tyr Asn Tyr Thr Gly Met  
35 40 45  
Gly Asn Ser Thr Asn Lys Lys Asp Ala Gln Ser Asn Ala Ala Arg Asp  
50 55 60  
Phe Val Asn Tyr Leu Val Arg Ile Asn Glu Ile Lys Ser Glu Glu Val  
65 70 75 80  
Pro Ala Phe Gly Val Ala Ser Pro Pro Pro Leu Thr Asp Thr Pro Asp  
85 90 95  
Thr Thr Ala Asn  
100

<210> 199  
<211> 127  
<212> PRT  
<213> Homo sapien

<400> 199

Met Val Lys Glu Thr Thr Tyr Tyr Asp Val Leu Gly Val Lys Pro Asn  
1 5 10 15  
Ala Thr Gln Glu Glu Leu Lys Lys Ala Tyr Arg Lys Leu Ala Leu Lys  
20 25 30  
Tyr His Pro Asp Lys Asn Pro Asn Glu Gly Glu Lys Phe Lys Gln Ile  
35 40 45  
Ser Gln Ala Tyr Glu Val Leu Ser Asp Ala Lys Lys Arg Glu Leu Tyr  
50 55 60  
Asp Lys Gly Gly Glu Gln Ala Ile Lys Glu Gly Gly Ala Gly Gly Gly  
65 70 75 80  
Phe Gly Ser Pro Met Asp Ile Phe Asp Met Phe Phe Gly Gly Gly Gly  
85 90 95  
Arg Met Gln Arg Glu Arg Arg Gly Lys Asn Val Val His Gln Leu Ser  
100 105 110  
Val Thr Leu Glu Asp Leu Tyr Asn Gly Ala Thr Arg Lys Leu Ala  
115 120 125

<210> 200  
<211> 90  
<212> PRT  
<213> Homo sapien

<400> 200

Met Ala Cys Pro Leu Asp Gln Ala Ile Gly Leu Leu Val Ala Ile Phe  
1 5 10 15

His Lys Tyr Ser Gly Arg Glu Gly Asp Lys His Thr Leu Ser Lys Lys  
 20 25 30  
 Glu Leu Lys Glu Leu Ile Gln Lys Glu Leu Thr Ile Gly Ser Lys Leu  
 35 40 45  
 Gln Asp Ala Glu Ile Ala Arg Leu Met Glu Asp Leu Asp Arg Asn Lys  
 50 55 60  
 Asp Gln Glu Val Asn Phe Gln Glu Tyr Val Thr Phe Leu Gly Ala Leu  
 65 70 75 80  
 Ala Leu Ile Tyr Asn Glu Ala Leu Lys Gly  
 85 90

<210> 201  
 <211> 120  
 <212> PRT  
 <213> Homo sapien

<400> 201  
 Met Glu Thr Pro Ser Gln Arg Arg Ala Thr Arg Ser Gly Ala Gln Ala  
 1 5 10 15  
 Ser Ser Thr Pro Leu Ser Pro Thr Arg Ile Thr Arg Leu Gln Glu Lys  
 20 25 30  
 Glu Asp Leu Gln Glu Leu Asn Asp Arg Leu Ala Val Tyr Ile Asp Arg  
 35 40 45  
 Val Arg Ser Leu Glu Thr Glu Asn Ala Gly Leu Arg Leu Arg Ile Thr  
 50 55 60  
 Glu Ser Glu Glu Val Val Ser Arg Glu Val Ser Gly Ile Lys Ala Ala  
 65 70 75 80  
 Tyr Glu Ala Glu Leu Gly Asp Ala Arg Lys Thr Leu Asp Ser Val Ala  
 85 90 95  
 Lys Glu Arg Ala Arg Leu Gln Leu Glu Leu Ser Lys Val Arg Glu Glu  
 100 105 110  
 Phe Lys Glu Leu Lys Ala Arg Asn  
 115 120

<210> 202  
 <211> 177  
 <212> PRT  
 <213> Homo sapien

<400> 202  
 Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Ile  
 1 5 10 15  
 Lys Met Glu Glu Glu Ser Gly Ala Pro Gly Val Pro Ser Gly Asn Gly  
 20 25 30  
 Ala Pro Gly Pro Lys Gly Glu Gly Glu Arg Pro Ala Gln Asn Glu Lys  
 35 40 45  
 Arg Lys Glu Lys Asn Ile Lys Arg Gly Gly Asn Arg Phe Glu Pro Tyr  
 50 55 60  
 Ala Asn Pro Thr Lys Arg Tyr Arg Ala Phe Ile Thr Asn Ile Pro Phe  
 65 70 75 80  
 Asp Val Lys Trp Gln Ser Leu Lys Asp Leu Val Lys Glu Lys Val Gly  
 85 90 95  
 Glu Val Thr Tyr Val Glu Leu Leu Met Asp Ala Glu Gly Lys Ser Arg  
 100 105 110  
 Gly Cys Ala Val Val Glu Phe Lys Met Glu Glu Ser Met Lys Lys Ala

115 120 125  
 Ala Glu Val Leu Asn Lys His Ser Leu Ser Gly Arg Pro Leu Lys Val  
 130 135 140  
 Lys Glu Asp Pro Asp Gly Glu His Ala Arg Arg Ala Met Gln Lys Ala  
 145 150 155 160  
 Gly Arg Leu Gly Ser Thr Val Phe Val Ala Asn Leu Asp Tyr Lys Val  
 165 170 175  
 Gly

<210> 203  
 <211> 164  
 <212> PRT  
 <213> Homo sapien

<400> 203  
 Met Arg Leu Ala Val Gly Ala Leu Leu Val Cys Ala Val Leu Gly Leu  
 1 5 10 15  
 Cys Leu Ala Val Pro Asp Lys Thr Val Arg Trp Cys Ala Val Ser Glu  
 20 25 30  
 His Glu Ala Thr Lys Cys Gln Ser Phe Arg Asp His Met Lys Ser Val  
 35 40 45  
 Ile Pro Ser Asp Gly Pro Ser Val Ala Cys Val Lys Lys Ala Ser Tyr  
 50 55 60  
 Leu Asp Cys Ile Arg Ala Ile Ala Ala Asn Glu Ala Asp Ala Val Thr  
 65 70 75 80  
 Leu Asp Ala Gly Leu Val Tyr Asp Ala Tyr Leu Ala Pro Asn Asn Leu  
 85 90 95  
 Lys Pro Val Val Ala Glu Phe Tyr Gly Ser Lys Glu Asp Pro Gln Thr  
 100 105 110  
 Phe Tyr Tyr Ala Val Ala Val Val Lys Lys Asp Ser Gly Phe Gln Met  
 115 120 125  
 Asn Gln Leu Arg Gly Lys Lys Ser Cys His Thr Gly Leu Gly Arg Ser  
 130 135 140  
 Ala Gly Trp Asn Ile Pro Ile Gly Leu Leu Tyr Cys Asp Leu Pro Glu  
 145 150 155 160  
 Pro Arg Lys Pro

<210> 204  
 <211> 241  
 <212> PRT  
 <213> Homo sapien

<400> 204  
 Met Ser Gly Glu Ser Ala Arg Ser Leu Gly Lys Gly Ser Ala Pro Pro  
 1 5 10 15  
 Gly Pro Val Pro Glu Gly Ser Ile Arg Ile Tyr Ser Met Arg Phe Cys  
 20 25 30  
 Pro Phe Ala Glu Arg Thr Arg Leu Val Leu Lys Ala Lys Gly Ile Arg  
 35 40 45  
 His Glu Val Ile Asn Ile Asn Leu Lys Asn Lys Pro Glu Trp Phe Phe  
 50 55 60  
 Lys Lys Asn Pro Phe Gly Leu Val Pro Val Leu Glu Asn Ser Gln Gly  
 65 70 75 80

<210> 205  
<211> 160  
<212> PRT  
<213> Homo sapien

**<400>. 205**

Met	Gln	Ile	Phe	Val	Lys	Thr	Leu	Thr	Gly	Lys	Thr	Ile	Thr	Leu	Glu
1				5					10					15	
Val	Glu	Pro	Ser	Asp	Thr	Ile	Glu	Asn	Val	Lys	Ala	Lys	Ile	Gln	Asp
			20					25					30		
Lys	Glu	Gly	Ile	Pro	Pro	Asp	Gln	Gln	Arg	Leu	Ile	Phe	Ala	Gly	Lys
		35					40					45			
Gln	Leu	Glu	Asp	Gly	Arg	Thr	Leu	Ser	Asp	Tyr	Asn	Ile	Gln	Lys	Glu
		50				55				60					
Ser	Thr	Leu	His	Leu	Val	Leu	Arg	Leu	Arg	Gly	Gly	Met	Gln	Ile	Phe
65					70					75					80
Val	Lys	Thr	Leu	Thr	Gly	Lys	Thr	Ile	Thr	Leu	Glu	Val	Glu	Pro	Ser
				85					90					95	
Asp	Thr	Ile	Glu	Asn	Val	Lys	Ala	Lys	Ile	Gln	Asp	Lys	Glu	Gly	Ile
			100					105					110		
Pro	Pro	Asp	Gln	Gln	Arg	Leu	Ile	Phe	Ala	Gly	Lys	Gln	Leu	Glu	Asp
		115					120					125			
Gly	Arg	Thr	Leu	Ser	Asp	Tyr	Asn	Ile	Gln	Lys	Glu	Ser	Thr	Leu	His
		130				135					140				
Leu	Val	Leu	Arg	Leu	Arg	Gly	Gly	Met	Gln	Ile	Phe	Val	Lys	Thr	Leu
145					150						155				160

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<210> 206
<211> 197
<212> PRT
<213> Homo sapien
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&lt;400&gt; 206

Thr Ser Pro Ser Glu Ala Cys Ala Pro Leu Leu Ile Ser Leu Ser Thr  
 1 5 10 15  
 Leu Ile Tyr Asn Gly Ala Leu Pro Cys Gln Cys Asn Pro Gln Gly Ser  
 20 25 30  
 Leu Ser Ser Glu Cys Asn Pro His Gly Gly Gln Cys Leu Cys Lys Pro  
 35 40 45  
 Gly Val Val Gly Arg Arg Cys Asp Leu Cys Ala Pro Gly Tyr Tyr Gly  
 50 55 60  
 Phe Gly Pro Thr Gly Cys Gln Gly Ala Cys Leu Gly Cys Arg Asp His  
 65 70 75 80  
 Thr Gly Gly Glu His Cys Glu Arg Cys Ile Ala Gly Phe His Gly Asp  
 85 90 95  
 Pro Arg Leu Pro Tyr Gly Gly Gln Cys Arg Pro Cys Pro Cys Pro Glu  
 100 105 110  
 Gly Pro Gly Ser Gln Arg His Phe Ala Thr Ser Cys His Gln Asp Glu  
 115 120 125  
 Tyr Ser Gln Gln Ile Val Cys His Cys Arg Ala Gly Tyr Thr Gly Leu  
 130 135 140  
 Arg Cys Glu Ala Cys Ala Pro Gly His Phe Gly Asp Pro Ser Arg Pro  
 145 150 155 160  
 Gly Gly Arg Cys Gln Leu Cys Glu Cys Ser Gly Asn Ile Asp Pro Met  
 165 170 175  
 Asp Pro Asp Ala Cys Asp Pro His Thr Gly Gln Cys Leu Arg Cys Leu  
 180 185 190  
 His His Thr Glu Gly  
 195

&lt;210&gt; 207

&lt;211&gt; 175

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 207

Ile Ile Arg Gln Gln Gly Leu Ala Ser Tyr Asp Tyr Val Arg Arg Arg  
 1 5 10 15  
 Leu Thr Ala Glu Asp Leu Phe Glu Ala Arg Ile Ile Ser Leu Glu Thr  
 20 25 30  
 Tyr Asn Leu Leu Arg Glu Gly Thr Arg Ser Leu Arg Glu Ala Leu Glu  
 35 40 45  
 Ala Glu Ser Ala Trp Cys Tyr Leu Tyr Gly Thr Gly Ser Val Ala Gly  
 50 55 60  
 Val Tyr Leu Pro Gly Ser Arg Gln Thr Leu Ser Ile Tyr Gln Ala Leu  
 65 70 75 80  
 Lys Lys Gly Leu Leu Ser Ala Glu Val Ala Arg Leu Leu Leu Glu Ala  
 85 90 95  
 Gln Ala Ala Thr Gly Phe Leu Leu Asp Pro Val Lys Gly Glu Arg Leu  
 100 105 110  
 Thr Val Asp Glu Ala Val Arg Lys Gly Leu Val Gly Pro Glu Leu His  
 115 120 125  
 Asp Arg Leu Leu Ser Ala Glu Arg Ala Val Thr Gly Tyr Arg Asp Pro  
 130 135 140  
 Tyr Thr Glu Gln Thr Ile Ser Leu Phe Gln Ala Met Lys Lys Glu Leu  
 145 150 155 160  
 Ile Pro Thr Glu Glu Ala Leu Arg Leu Trp Met Pro Ser Trp Pro

109

165

170

175

<210> 208  
 <211> 177  
 <212> PRT  
 <213> Homo sapien

&lt;400&gt; 208

Met Ala Ala Gly Val Glu Ala Ala Ala Glu Val Ala Ala Thr Glu Ile  
 1 5 10 15  
 Lys Met Glu Glu Ser Gly Ala Pro Gly Val Pro Ser Gly Asn Gly  
 20 25 30  
 Ala Pro Gly Pro Lys Gly Glu Gly Glu Arg Pro Ala Gln Asn Glu Lys  
 35 40 45  
 Arg Lys Glu Lys Asn Ile Lys Arg Gly Gly Asn Arg Phe Glu Pro Tyr  
 50 55 60  
 Ala Asn Pro Thr Lys Arg Tyr Arg Ala Phe Ile Thr Asn Ile Pro Phe  
 65 70 75 80  
 Asp Val Lys Trp Gln Ser Leu Lys Asp Leu Val Lys Glu Lys Val Gly  
 85 90 95  
 Glu Val Thr Tyr Val Glu Leu Leu Met Asp Ala Glu Gly Lys Ser Arg  
 100 105 110  
 Gly Cys Ala Val Val Glu Phe Lys Met Glu Glu Ser Met Lys Lys Ala  
 115 120 125  
 Ala Glu Val Leu Asn Lys His Ser Leu Ser Gly Arg Pro Leu Lys Val  
 130 135 140  
 Lys Glu Asp Pro Asp Gly Glu His Ala Arg Arg Ala Met Gln Lys Val  
 145 150 155 160  
 Met Ala Thr Thr Gly Gly Met Gly Met Gly Pro Gly Gly Pro Gly Met  
 165 170 175  
 Ile

<210> 209  
 <211> 196  
 <212> PRT  
 <213> Homo sapien

&lt;400&gt; 209

Asp Leu Gln Asp Met Phe Ile Val His Thr Ile Glu Glu Ile Glu Gly  
 1 5 10 15  
 Leu Ile Ser Ala His Asp Gln Phe Lys Ser Thr Leu Pro Asp Ala Asp  
 20 25 30  
 Arg Glu Arg Glu Ala Ile Leu Ala Ile His Lys Glu Ala Gln Arg Ile  
 35 40 45  
 Ala Glu Ser Asn His Ile Lys Leu Ser Gly Ser Asn Pro Tyr Thr Thr  
 50 55 60  
 Val Thr Pro Gln Ile Ile Asn Ser Lys Trp Glu Lys Val Gln Gln Leu  
 65 70 75 80  
 Val Pro Lys Arg Asp His Ala Leu Leu Glu Glu Gln Ser Lys Gln Gln  
 85 90 95  
 Ser Asn Glu His Leu Arg Arg Gln Phe Ala Ser Gln Ala Asn Val Val  
 100 105 110  
 Gly Pro Trp Ile Gln Thr Lys Met Glu Glu Ile Gly Arg Ile Ser Ile  
 115 120 125

Glu Met Asn Gly Thr Leu Glu Asp Gln Leu Ser His Leu Lys Gln Tyr  
 130 135 140  
 Glu Arg Ser Ile Val Asp Tyr Lys Pro Asn Leu Asp Leu Leu Glu Gln  
 145 150 155 160  
 Gln His Gln Leu Ile Gln Glu Ala Leu Ile Phe Asp Asn Lys His Thr  
 165 170 175  
 Asn Tyr Thr Met Glu His Ile Arg Val Gly Trp Glu Gln Leu Thr  
 180 185 190  
 Thr Ile Ala Arg  
 195

&lt;210&gt; 210

&lt;211&gt; 156

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 210

Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly Lys Glu  
 1 5 10 15  
 Val Leu Leu Leu Ala His Asn Leu Pro Gln Asn Arg Ile Gly Tyr Ser  
 20 25 30  
 Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Ser Leu Ile Val Gly Tyr  
 35 40 45  
 Val Ile Gly Thr Gln Gln Ala Thr Pro Gly Pro Ala Tyr Ser Gly Arg  
 50 55 60  
 Glu Thr Ile Tyr Pro Asn Ala Ser Leu Leu Ile Gln Asn Val Thr Gln  
 65 70 75 80  
 Asn Asp Thr Gly Phe Tyr Thr Leu Gln Val Ile Lys Ser Asp Leu Val  
 85 90 95  
 Asn Glu Glu Ala Thr Gly Gln Phe His Val Tyr Pro Glu Leu Pro Lys  
 100 105 110  
 Pro Ser Ile Ser Ser Asn Asn Ser Asn Pro Val Glu Asp Lys Asp Ala  
 115 120 125  
 Val Ala Phe Thr Cys Glu Pro Glu Val Gln Asn Thr Thr Tyr Leu Trp  
 130 135 140  
 Trp Val Asn Gly Gln Ser Leu Pro Val Ser Pro Lys  
 145 150 155

&lt;210&gt; 211

&lt;211&gt; 92

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 211

Met Glu Ser Pro Ser Ala Pro Pro His Arg Trp Cys Ile Pro Trp Gln  
 1 5 10 15  
 Arg Leu Leu Leu Thr Ala Ser Leu Leu Thr Phe Trp Asn Pro Pro Thr  
 20 25 30  
 Thr Ala Lys Leu Thr Ile Glu Ser Thr Pro Phe Asn Val Ala Glu Gly  
 35 40 45  
 Lys Glu Val Leu Leu Leu Val His Asn Leu Pro Gln His Leu Phe Gly  
 50 55 60  
 Tyr Ser Trp Tyr Lys Gly Glu Arg Val Asp Gly Asn Arg Gln Ile Ile  
 65 70 75 80  
 Gly Tyr Val Ile Gly Thr Gln Gln Ala Thr Pro Gly

85

90

<210> 212  
 <211> 142  
 <212> PRT  
 <213> Homo sapien

&lt;400&gt; 212

Glu Lys Gln Lys Asn Lys Glu Phe Ser Gln Thr Leu Glu Asn Glu Lys  
 1 5 10 15  
 Asn Thr Leu Leu Ser Gln Ile Ser Thr Lys Asp Gly Glu Leu Lys Met  
 20 25 30  
 Leu Gln Glu Glu Val Thr Lys Met Asn Leu Leu Asn Gln Gln Ile Gln  
 35 40 45  
 Glu Glu Leu Ser Arg Val Thr Lys Leu Lys Glu Thr Ala Glu Glu Glu  
 50 55 60  
 Lys Asp Asp Leu Glu Glu Arg Leu Met Asn Gln Leu Ala Glu Leu Asn  
 65 70 75 80  
 Gly Ser Ile Gly Asn Tyr Cys Gln Asp Val Thr Asp Ala Gln Ile Lys  
 85 90 95  
 Asn Glu Leu Leu Glu Ser Glu Met Lys Asn Leu Lys Lys Cys Val Ser  
 100 105 110  
 Glu Leu Glu Glu Lys Gln Gln Leu Val Lys Glu Lys Thr Lys Val  
 115 120 125  
 Glu Ser Glu Ile Arg Lys Glu Tyr Leu Glu Lys Ile Gln Gly  
 130 135 140

<210> 213  
 <211> 142  
 <212> PRT  
 <213> Homo sapien

&lt;400&gt; 213

Gly Gly Tyr Gly Gly Tyr Gly Gly Val Leu Thr Ala Ser Asp Gly  
 1 5 10 15  
 Leu Leu Ala Gly Asn Glu Lys Leu Thr Met Gln Asn Leu Asn Asp Arg  
 20 25 30  
 Leu Ala Ser Tyr Leu Asp Lys Val Arg Ala Leu Glu Ala Ala Asn Gly  
 35 40 45  
 Glu Leu Glu Val Lys Ile Arg Asp Trp Tyr Gln Lys Gln Gly Pro Gly  
 50 55 60  
 Pro Ser Arg Asp Tyr Ser His Tyr Tyr Thr Thr Ile Gln Asp Leu Arg  
 65 70 75 80  
 Asp Lys Ile Leu Gly Ala Thr Ile Glu Asn Ser Arg Ile Val Leu Gln  
 85 90 95  
 Ile Asp Asn Ala Arg Leu Ala Ala Asp Asp Phe Arg Thr Lys Phe Glu  
 100 105 110  
 Thr Glu Gln Ala Leu Arg Met Ser Val Glu Ala Asp Ile Asn Gly Leu  
 115 120 125  
 Arg Arg Val Leu Asp Glu Leu Thr Leu Ala Arg Thr Asp Leu  
 130 135 140

<210> 214  
 <211> 129  
 <212> PRT



&lt;213&gt; Homo sapien

&lt;400&gt; 214

Val Met Arg Val Asp Phe Asn Val Pro Met Lys Asn Asn Gln Ile Thr  
 1 5 10 15  
 Asn Asn Gln Arg Ile Lys Ala Ala Val Pro Ser Ile Lys Phe Cys Leu  
 20 25 30  
 Asp Asn Gly Ala Lys Ser Val Val Leu Met Ser His Leu Gly Arg Pro  
 35 40 45  
 Asp Gly Val Pro Met Pro Asp Lys Tyr Ser Leu Glu Pro Val Ala Val  
 50 55 60  
 Glu Leu Arg Ser Leu Leu Gly Lys Asp Val Leu Phe Leu Lys Asp Cys  
 65 70 75 80  
 Val Gly Pro Glu Val Glu Lys Ala Cys Ala Asn Pro Ala Ala Gly Ser  
 85 90 95  
 Val Ile Leu Leu Glu Asn Leu Arg Phe His Val Glu Glu Glu Lys  
 100 105 110  
 Gly Lys Asp Ala Ser Gly Asn Lys Val Lys Ala Glu Pro Ala Lys Ile  
 115 120 125  
 Glu

&lt;210&gt; 215

&lt;211&gt; 148

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 215

Met Ala Thr Leu Lys Glu Lys Leu Ile Ala Pro Val Ala Glu Glu Glu  
 1 5 10 15  
 Ala Thr Val Pro Asn Asn Lys Ile Thr Val Val Gly Val Gly Gln Val  
 20 25 30  
 Gly Met Ala Cys Ala Ile Ser Ile Leu Gly Lys Ser Leu Ala Asp Glu  
 35 40 45  
 Leu Ala Leu Val Asp Val Leu Glu Asp Lys Leu Lys Gly Glu Met Met  
 50 55 60  
 Asp Leu Gln His Gly Ser Leu Phe Leu Gln Thr Pro Lys Ile Val Ala  
 65 70 75 80  
 Asp Lys Asp Tyr Ser Val Thr Ala Asn Ser Lys Ile Val Val Val Thr  
 85 90 95  
 Ala Gly Val Arg Gln Gln Glu Gly Glu Ser Arg Leu Asn Leu Val Gln  
 100 105 110  
 Arg Asn Val Asn Val Phe Lys Phe Ile Ile Pro Gln Ile Val Lys Tyr  
 115 120 125  
 Ser Pro Asp Cys Ile Ile Ile Val Val Ser Asn Pro Val Asp Ile Leu  
 130 135 140  
 Thr Tyr Val Thr  
 145

&lt;210&gt; 216

&lt;211&gt; 527

&lt;212&gt; PRT

&lt;213&gt; Homo sapien

&lt;400&gt; 216

Gln Arg Ala Pro Gly Ile Glu Glu Lys Ala Ala Glu Asn Gly Ala Leu  
 1 5 10 15  
 Gly Ser Pro Glu Arg Glu Glu Lys Val Leu Glu Asn Gly Glu Leu Thr  
 20 25 30  
 Pro Pro Arg Arg Glu Glu Lys Ala Leu Glu Asn Gly Glu Leu Arg Ser  
 35 40 45  
 Pro Glu Ala Gly Glu Lys Val Leu Val Asn Gly Gly Leu Thr Pro Pro  
 50 55 60  
 Lys Ser Glu Asp Lys Val Ser Glu Asn Gly Gly Leu Arg Phe Pro Arg  
 65 70 75 80  
 Asn Thr Glu Arg Pro Pro Glu Thr Gly Pro Trp Arg Ala Pro Gly Pro  
 85 90 95  
 Trp Glu Lys Thr Pro Glu Ser Trp Gly Pro Ala Pro Thr Ile Gly Glu  
 100 105 110  
 Pro Ala Pro Glu Thr Ser Leu Glu Arg Ala Pro Ala Pro Ser Ala Val  
 115 120 125  
 Val Ser Ser Arg Asn Gly Gly Glu Thr Ala Pro Gly Pro Leu Gly Pro  
 130 135 140  
 Ala Pro Lys Asn Gly Thr Leu Glu Pro Gly Thr Glu Arg Arg Ala Pro  
 145 150 155 160  
 Glu Thr Gly Gly Ala Pro Arg Ala Pro Gly Ala Gly Arg Leu Asp Leu  
 165 170 175  
 Gly Ser Gly Gly Arg Ala Pro Val Gly Thr Gly Thr Ala Pro Gly Gly  
 180 185 190  
 Gly Pro Gly Ser Gly Val Asp Ala Lys Ala Gly Trp Val Asp Asn Thr  
 195 200 205  
 Arg Pro Gln Pro Pro Pro Pro Pro Leu Pro Pro Pro Glu Ala Gln  
 210 215 220  
 Pro Arg Arg Leu Glu Pro Ala Pro Pro Arg Ala Arg Pro Glu Val Ala  
 225 230 235 240  
 Pro Glu Gly Glu Pro Gly Ala Pro Asp Ser Arg Ala Gly Gly Asp Thr  
 245 250 255  
 Ala Leu Ser Gly Asp Gly Asp Pro Pro Lys Pro Glu Arg Lys Gly Pro  
 260 265 270  
 Glu Met Pro Arg Leu Phe Leu Asp Leu Gly Pro Pro Gln Gly Asn Ser  
 275 280 285  
 Glu Gln Ile Lys Ala Arg Leu Ser Arg Leu Ser Leu Ala Leu Pro Pro  
 290 295 300  
 Leu Thr Leu Thr Pro Phe Pro Gly Pro Gly Pro Arg Arg Pro Pro Trp  
 305 310 315 320  
 Glu Gly Ala Asp Ala Gly Ala Ala Gly Gly Glu Ala Gly Gly Ala Gly  
 325 330 335  
 Ala Pro Gly Pro Ala Glu Glu Asp Gly Glu Asp Glu Asp Glu Asp Glu  
 340 345 350  
 Glu Glu Asp Glu Glu Ala Ala Ala Pro Gly Ala Ala Ala Gly Pro Arg  
 355 360 365  
 Gly Pro Gly Arg Ala Arg Ala Ala Pro Val Pro Val Val Val Ser Ser  
 370 375 380  
 Ala Asp Ala Asp Ala Ala Arg Pro Leu Arg Gly Leu Leu Lys Ser Pro  
 385 390 395 400  
 Arg Gly Ala Asp Glu Pro Glu Asp Ser Glu Leu Glu Arg Lys Arg Lys  
 405 410 415  
 Met Val Ser Phe His Gly Asp Val Thr Val Tyr Leu Phe Asp Gln Glu  
 420 425 430  
 Thr Pro Thr Asn Glu Leu Ser Val Gln Ala Pro Pro Glu Gly Asp Thr

435 440 445  
Asp Pro Ser Thr Pro Pro Ala Pro Pro Thr Pro Pro His Pro Ala Thr  
450 455 460  
Pro Gly Asp Gly Phe Pro Ser Asn Asp Ser Gly Phe Gly Gly Ser Phe  
465 470 475 480  
Glu Trp Ala Glu Asp Phe Pro Leu Leu Pro Pro Pro Gly Pro Pro Leu  
485 490 495  
Cys Phe Ser Arg Phe Ser Val Ser Pro Ala Leu Glu Thr Pro Gly Pro  
500 505 510  
Pro Ala Arg Ala Pro Asp Ala Arg Pro Ala Gly Pro Val Glu Asn  
515 520 525

**PCT**WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : C12N 15/12, A61K 38/17, C07K 14/47, 16/18, A61K 35/14		A3	(11) International Publication Number: <b>WO 99/38973</b> (43) International Publication Date: 5 August 1999 (05.08.99)
(21) International Application Number: PCT/US99/01642 (22) International Filing Date: 26 January 1999 (26.01.99) (30) Priority Data: 09/015,029 28 January 1998 (28.01.98) US 09/015,022 28 January 1998 (28.01.98) US 09/040,828 18 March 1998 (18.03.98) US 09/040,831 18 March 1998 (18.03.98) US 09/122,192 23 July 1998 (23.07.98) US 09/122,191 23 July 1998 (23.07.98) US 09/219,245 22 December 1998 (22.12.98) US		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(71) Applicant: CORIXA CORPORATION [US/US]; Suite 200, 1124 Columbia Street, Seattle, WA 98104 (US). (72) Inventors: REED, Steven, G.; 2843 - 122nd Place N.E., Bellevue, WA 98005 (US). LODES, Michael, J.; 9223 - 36th Avenue S.W., Seattle, WA 98126 (US). FRUDAKIS, Tony, N.; P.O. Box 99232, Seattle, WA 99232-0232 (US). MOHAMATH, Raodoh; 4205 South Morgan, Seattle, WA 98118 (US). (74) Agents: MAKI, David, J. et al.; Seed and Berry LLP, 6300 Columbia Center, 701 Fifth Avenue, Seattle, WA 98104-7092 (US).		Published With international search report. * Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments. (88) Date of publication of the international search report: 9 December 1999 (09.12.99)	
(54) Title: COMPOUNDS FOR THERAPY AND DIAGNOSIS OF LUNG CANCER AND METHODS FOR THEIR USE			
(57) Abstract <p>Compounds and methods for treating lung cancer are provided. The inventive compounds include polypeptides containing at least a portion of a lung tumor protein. Vaccines and pharmaceutical compositions for immunotherapy of lung cancer comprising such polypeptides, or polynucleotides encoding such polypeptides, are also provided, together with polynucleotides for preparing the inventive polypeptides.</p>			

# INTERNATIONAL SEARCH REPORT

International Application No.  
PCT/US 99/01642

<b>A. CLASSIFICATION OF SUBJECT MATTER</b> IPC 6 C12N15/12 A61K38/17 C07K14/47 C07K16/18 A61K35/14		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b> Minimum documentation searched (classification system followed by classification symbols) IPC 6 C12N C12Q A61K C07K		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practical, search terms used)		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 96 30389 A (MILLENNIUM PHARMACEUTICALS, INC.; SHYJAN A.) 3 October 1996 see page 112 - page 127 ---	1-60
A	WO 96 02552 A (CYTOCLONYL PHARMACEUTICS, INC.; TORCZYNSKI R. ET AL.) 1 February 1996 see the whole document ---	1-60
A	YOU L ET AL.: "Identification of early growth response gene-1 (Egr-1) as a phorbol myristate-induced gene in lung cancer cells by differential mRNA display" AM. J. RESPIR. CELL MOL. BIOL., vol. 17, no. 5, November 1997, pages 617-624, XP002106654 see page 618, left-hand column, paragraph 3 --- <div style="text-align: right;">-/-</div>	1,2,4-7
<div style="display: flex; justify-content: space-between;"> <span><input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.</span> <span><input checked="" type="checkbox"/> Patent family members are listed in annex.</span> </div>		
* Special categories of cited documents :		
<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone</p> <p>"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"Z" document member of the same patent family</p> </div> </div>		
Date of the actual completion of the international search  <div style="text-align: center;">21 June 1999</div>		Date of mailing of the international search report  <div style="text-align: center;">22 10 1999</div>
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016		Authorized officer  <div style="text-align: center;">CUPIDO, M</div>

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 99/01642

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
Remark: Although claims 16, 17, 24-26, 32, 33, 48-53 and 56-58 are directed to a method of treatment of the human/animal body the search has been carried out and based on the alleged effects of the composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see FURTHER INFORMATION sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see FURTHER INFORMATION sheet, subject 1.

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 99/01642

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9630389 A	03-10-1996	US 5633161 A	27-05-1997
		AU 708746 B	12-08-1999
		AU 5437896 A	16-10-1996
		CA 2216717 A	03-10-1996
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		US 5773579 A	30-06-1998